Thomas Jefferson University

Jefferson Digital Commons

Department of Pharmacology and Experimental Therapeutics Faculty Papers

Department of Pharmacology and Experimental Therapeutics

5-9-2013

The Impact of Community Use of Novel Oral Anticoagulants on an Academic Medical Center

Luis Eraso, MD
Thomas Jefferson University Hospital

Taki Galanis, MD
Thomas Jefferson University Hospital

Kristina Kipp, Pharm.D.
Thomas Jefferson University Hospital

Walter K. Kraft, MD
Thomas Jefferson University Hospital

Michael Palladino, Pharm.D., CACP
Thomas Jefferson University Hospital

Follow this and additional works at: https://jdc.jefferson.edu/petfp

Part of the Medicinal and Pharmaceutical Chemistry Commons, Nursing Commons, and the Pharmacy and Pharmaceutical Sciences Commons

Let us know how access to this document benefits you

See next page for additional authors

Recommended Citation

Eraso, MD, Luis; Galanis, MD, Taki; Kipp, Pharm.D., Kristina; Kraft, MD, Walter K.; Palladino, Pharm.D., CACP, Michael; Perez, MD, Alejandro; Ferebee-Spruill, CRNP, Kimberle; Merli, MD, Geno; Swift, Pharm.D., MBA, Brian G.; Thomson, Lynda; and Vining, Brittany, "The Impact of Community Use of Novel Oral Anticoagulants on an Academic Medical Center" (2013). *Department of Pharmacology and Experimental Therapeutics Faculty Papers.* Paper 42.
https://jdc.jefferson.edu/petfp/42

This Article is brought to you for free and open access by the Jefferson Digital Commons. The Jefferson Digital Commons is a service of Thomas Jefferson University's Center for Teaching and Learning (CTL). The Commons is a showcase for Jefferson books and journals, peer-reviewed scholarly publications, unique historical collections from the University archives, and teaching tools. The Jefferson Digital Commons allows researchers and interested readers anywhere in the world to learn about and keep up to date with Jefferson scholarship. This article has been accepted for inclusion in Department of Pharmacology and Experimental Therapeutics Faculty Papers by an authorized administrator of the Jefferson Digital Commons. For more information, please contact: JeffersonDigitalCommons@jefferson.edu.

Authors

Luis Eraso, MD; Taki Galanis, MD; Kristina Kipp, Pharm.D.; Walter K. Kraft, MD; Michael Palladino, Pharm.D., CACP; Alejandro Perez, MD; Kimberle Ferebee-Spruill, CRNP; Geno Merli, MD; Brian G. Swift, Pharm.D., MBA; Lynda Thomson; and Brittany Vining

This poster is available at Jefferson Digital Commons: https://jdc.jefferson.edu/petfp/42

The Impact of Community Use of Novel Oral Anticoagulants on an Academic Medical Center

Luis Eraso, M.D, Taki Galanis, M.D., Kristina Kipp, Pharm.D., Walter K. Kraft, M.D., Michael Palladino, Pharm.D., Alejandro Perez, MD., Kimberle Ferebee – Spruill, CRNP, Geno Merli, M,D., Brian Swift, Pharm.D., Lynda Thomson, Pharm.D, Brittany Vining.

Thomas Jefferson University Hospital, Philadelphia, PA, United States

Presenters: Alyssa Gumkowski, Geno Merli, M.D., Kimberle Ferebee-Spruill, CRNP

Introduction:

Warfarin has been a mainstay of therapy for treatment and prevention of venous thromboembolic disease (VTED) and prevention of stroke and systemic embolism for over 50 years. Recent FDA approval of several novel oral anticoagulants has offered more extensive treatment options for management of these disease states.

Novel Anticoagulant	FDA Approval Date	Approved Indication
Dabigatran	October 19, 2010	Prevention of stroke and systemic embolism
Rivaroxaban	November 4, 2011	Prevention of stroke and systemic embolism
Apixaban	November 2, 2012	Treatment acute and chronic VTED
	December 28, 2012	Prevention of stroke and systemic embolism

The availability of the novel anticoagulants offers an attractive alternative to warfarin therapy for patients due to their convenience of use. In comparison to warfarin, dabigatran, rivaroxaban and apixaban offer:

- a fixed dosage regimen
- a relatively small potential drug interaction profile
- minimal laboratory monitoring
- little to no dietary restrictions.

Although these agents offer a relatively fixed dose regimen, dosage adjustment is required in moderate renal dysfunction, and use is contraindicated in severe renal dysfunction. Currently there are no specific reversal agents in the event of a novel anticoagulant associated bleed. These concerns led to the development of an anticoagulation stewardship program at our institution to monitor and guide the usage of these agents.

Background of the Program:

Thomas Jefferson University Hospital is a 957 licensed acute care bed academic medical center with 3 hospital locations in the Philadelphia area, including a facility in center city, South Philadelphia and a neuroscience hospital. Our neuroscience hospital, JHN, is the only hospital dedicated to the treatment of neurological diseases in the Philadelphia region, and receives a large number of transfers from hospitals within the tri-state area for management of intracranial hemorrhages, including those associated with anticoagulation use.

In an effort to insure the safe and appropriate use of the novel anticoagulants and timely management of admissions from the community for associated adverse events, a steering committee of specialized physicians and pharmacists met to develop a comprehensive management program, which includes:

- guidelines for use
- an educational program
- CPOE order sets
- a surveillance program
- monitoring criteria with recommended laboratory assays
- perioperative management guidelines
- emergency management response process

A care transitions program was also developed to insure proper communication of care plans and follow-up after discharge, and to, hopefully, prevent adverse events and readmissions.

Below are some examples of the program components

Dabigatran Inclusion and Exclusion Criteria

Approved by P&T Committee and Medical Executive Committee Spring 2011

New inpatient requests for dabigatran should be screened for appropriateness of use. Use of dabigatran not meeting inclusion criteria would require a consult from Cardiology, Vascular Medicine (JATS), or Cardeza to approve use in the inpatient setting.

A. Inclusion criteria:

Prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation

B. Exclusion criteria:

Patients with atrial fibrillation and history of mitral valve stenosis, valvuloplasty or rheumatic heart disease.

Infectious endocarditis

Patients with a previous stroke within the past 6 months

Conditions associated with an increased risk of bleeding, including, but not limited to:

- Major surgery within the past month
- History of intracranial, intraocular, spinal, retroperitoneal, gastrointestinal or atraumatic intra-articular bleeding
- History of a hemorrhagic disorder, including hemophilia
- Active malignancies of a highly vascular nature

Symptomatic or endoscopically documented gastroduodenal ulcer, Crohn's disease, ulcerative colitis or severe GERD

Pt unable to swallow an intact pill, such as patients with an enteral feeding tube

Uncontrolled hypertension (systolic blood pressure >180 mm Hg and/or diastolic blood pressure > 100 mm Hg)

Severe renal dysfunction (i.e. CrCl < 30 ml/min) or unstable renal function with declining urine output (<0.5 ml/kg/hr based on ideal body weight) in a patient with a baseline CrCl < 50 ml/min

Age < 18 years of age

Pregnant or nursing mothers

Active liver disease, including ALT, AST, Alk Phos > two times upper normal limits, active Hepatitis A,B,C

Clinically significant anemia (Hgb < 10g/dl)

Thrombocytopenia (platelet count < 100 X 10^3/L)

Known history of non-compliance

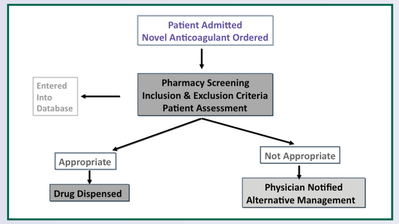
No prescription coverage or means to acquire medication

Concomitant use of Rifampin

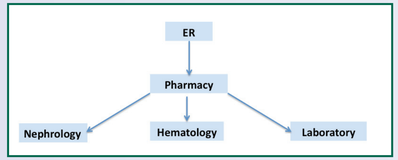
C. Relative Contraindications

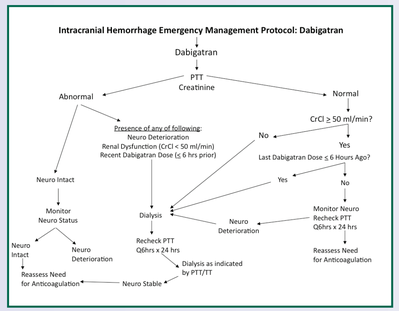
- Advanced age > 75 years of age
- Caution should be exercised in certain high risk populations, such as combined advanced age (>75 years), with low body weight and / or renal dysfunction (CrCl < 50 ml/min)
- Concomitant antiplatelet therapy: prasugrel, clopidogrel, aspirin or NSAIDS
- Pt requiring ongoing repeat interruption of therapy for invasive procedures, e.g. patient with ascites requiring repeat paracentesis procedures
- Concomitant therapy with other drugs known to be major p-glycoprotein inducers or inhibitors, e.g. amiodarone, quinidine
- Prior history of MI or unstable angina

Novel Anticoagulation Stewardship Program



Hospital Novel Anticoagulant Emergency Management Team



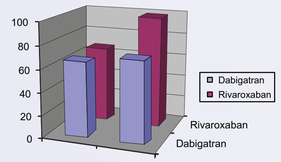


Our Experience

Impact of Community Prescribing on Our Institution:

The use of dabigatran, rivaroxaban and apixaban has resulted in increased workload on our pharmacy team to insure safe and appropriate utilization of these agents. The majority of interventions has occurred at time of admission, and mainly has involved either: suboptimal patient selection, dosing or inappropriate management in the perioperative period. A summary of the interventions are listed below.

Percentage of Novel Anticoagulant Orders Requiring Intervention



Dabigatran Surveillance Program (2 year period)

93% of all orders required an intervention

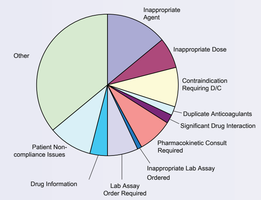
Average patient age: 73 yrs. **Age Range 35 – 90 yrs.**

Average patient weight: 83 kg **Weight Range: 40 – 179 kg**

Majority of interventions required in the "frail elderly" population

Frequent interventions included: switching to a more appropriate anticoagulant due to poor renal function, dosage adjustment and discontinuation of duplicate anticoagulants: e.g. subcutaneous heparin ordered for "DVT prophylaxis" with dabigatran.

Rivaroxaban Intervention by Type (%) N=67



Rivaroxaban Surveillance Program (1 year period)

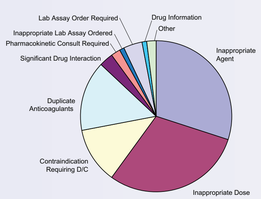
68 % of all orders required an intervention

Average patient age: 61 yrs. **Age Range 15 – 91 yrs.**

Average patient weight: 82 kg **Weight Range: 36 – 157 kg**

Majority of interventions required in the "frail elderly" population, requiring conversion to a more appropriate anticoagulant due to unstable and / or declining renal function, often in the setting of advanced CHF. Alteration in concomitant medication regimens required for contraindicated medications, including carbamazepine use in a patient being treated with rivaroxaban for a Saddle Pulmonary Embolism.

Dabigatran Orders Requiring Intervention by Type (%) N=71



Apixaban Surveillance Program: Implementation pending official approval for formulary addition

Adverse Events

As part of an ongoing quality and safety initiative, bleeding events associated with novel anticoagulant use are being monitored in hospitalized patients at our institution. All hemorrhagic events occurred within the community and resulted in an admission to our hospital system, mainly at our neuroscience hospital. A summary of these adverse events and cost of care is listed below:

Summary of Adverse Events and Patient Characteristics

8 patients were admitted to TJUH from November 2011 to May 2012 for bleeding, all were associated with dabigatran use. Six patients were transferred from an outside hospital to our neuroscience hospital for ICH management. All patients were on anticoagulation for atrial fibrillation, the most commonly prescribed dose of dabigatran was 150mg BID. Average pt age was 80.3 yrs. (range 63-90).

Average admission serum creatinine was 1.8 mg/dL (range 0.5-3.0). Female to Male 1:1. Strategies for the management of bleeding included withholding dabigatran, supportive care, administration of blood products and hemodialysis, when required. Dialysis was initiated on 3 patients, conventional +/ - CVVHD.

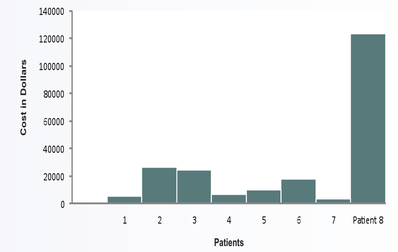
One patient died.

The average aPTT on admission was 69 seconds (range 32-170).

The average ICU length of stay was 10.4 days (range 0-39), with an average ICU cost of $28,883.75. Total inpatient cost averaged $46,603.00m with a cost range of $15,963.00 – 160,899.00. The average length of stay was 14 days (range 5-44).

Patient Case	Age & Gender	Scr (mg/dl)	Dabigatran Dose	Type of Bleed	aPTT at baseline (secs)	Time to normalize aPTT	Length of Stay	ICU LOS	Factor Products RX Received	Co-Morbidities	Other Outpatient Meds on Admission
1	76 M	1.1	150 mg BID	GU	85	Remained elevated	5	1	FFP Supportive	Alb. COPD HTN low-grade B lymphoma glaucoma	Amiodarone Digoxin Diltiazem Tamsulosin prn: Levalbuterol ipratropium Advair
2	79 M	3.1	75 mg BID	ICH	54	7 days	11	8	Hemodialysis, Supportive	HTN CAD CHF COPD	Amlodipine Flecainide Omeprazole
3	84 F	0.7	150 mg BID	ICH	60	4 days	17	9	Supportive	Parox Afib CAD HTN RA urticarial vasculitis	Amiodarone Duloxetine Famotidine Furosemide Hydrocortisone. Levetiracetam Metoprolol Multivitamin Mycophenolate Senna
4	87 F	3.9	150 mg BID	GI and epistaxis	170	March 1st 2012	5	4	2 units PRBC, Supportive	Acute renal failure Alb CAD HTN Hyperlipidemia COPD	Aspirin 81 mg daily Bumetanide Lovastatin Metolazone Metoprolol Olmesartan Trobymein
5	80F	0.9	150 mg BID	ICH/SAH	60	2 days	8	4	Hemodialysis X 2 sessions, Supportive	Afib CAD HTN Hx: Breast CA Melanoma Bilateral carotid stenosis	Aspirin 81 mg daily Celecoxib Diltiazem ER HCTZ, Lisinopril Metaxalone Vytorin/B
6	83 M	1.5	150 mg BID	SDH, cardiogenic shock	32	N/A	4	4	Supportive: Pressors, Intubation	Cardiomyopathy Severe AS Afib Outcome: Pt died	Amiodarone Carvedilol Furosemide Lisinopril Omeprazole
7	90 F	0.9	150 mg BID	SAH, SDH	39	N/A	18	15	Hemodialysis, Supportive	Anemia Afib CAD CRI, stage IV Depression GERD HTN Hyperlipidemia PSVT	Digoxin Dronedarone Escitalopram Metoprolol Mirtazepine
8	63 M	2.8	150 mg BID	GI / retro-peritoneal	48	2 days	44	39	Hemodialysis: CVVHD, Supportive, Pressors	Acute renal failure Afluttar CAD COPD V tach	Aspirin 81 mg daily Clopidogrel

ICU Cost



Total Cost of Care

As expected, the inpatient cost for caring for patients admitted with a novel anticoagulant associated bleeding event was high, with the highest costs incurred in patients admitted with an intracranial hemorrhage and those requiring hemodialysis for emergency management.

Average Total Cost of Care	Total Cost of Care Range
$46,603.00	$15,963.00 – 160,899.00

Conclusions:

The perceived ease of use of the novel anticoagulants has resulted in an increasingly popular utilization of these agents in the outpatient population as an alternative to warfarin therapy. These agents are frequently employed in the elderly population, since it is often difficult for this group of patients to go to their doctor's office or a laboratory for the required laboratory testing needed with warfarin management, mainly due to transportation and health issues.

These anticoagulants must be used with caution in certain subsets of patients, including the frail elderly or those with comorbidities which increase the risk for unstable and declining renal function. We have found that development and implementation of screening and educational tools were very useful in insuring appropriate patient selection by providing ongoing education to the house staff; we have experienced relatively little problems with new inpatient orders for these agents. Most of our efforts have involved adjustment and alteration of orders at the time of admission for patients chronically prescribed novel anticoagulants as outpatient therapy.

Experience from our stewardship program has shown that many orders from the community require alteration to another more optimal anticoagulant agent or adjustment of dose due to factors that increase the risk for drug accumulation and development of adverse events.

Novel anticoagulant adverse events can be difficult to manage and result in long ICU stays and high healthcare costs. Widespread use within the community has lead to increased workload on our pharmacy and medical staff to assess and adjust inappropriate usage. A formalized transition of care program is necessary to: insure appropriate monitoring and follow up after discharge, insure adequate communication of care plans to outpatient physicians, enhance patient understanding and compliance with treatment / follow-up, and insure optimal patient outcomes.