Mercy Heart & Vascular Institute

CARDIAC MONITOR

For healthcare professionals

Winter 2009

Medication advances help prevent stroke in atrial fibrillation

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Atrial fibrillation (AF) is the most common cardiac arrhythmia, currently estimated to affect 2 million people in the United States. It is also associated with a five-fold increase in the risk of stroke[1-3]. But the days of treating and preventing venous and arterial thromboembolic conditions with warfarin may be coming to an end. An alternative class of medications that can overcome the problematic drug interactions, dietary issues and narrow therapeutic range of warfarin is on the horizon. The newest class of oral anticoagulants — direct thrombin inhibitors (DTIs) and indirect factor Xa inhibitors (FXaI) — are here.

Warfarin, a vitamin K antagonist, reduces the AF-related stroke risk by 68% and is superior to both aspirin and clopidogrel for this indication[3]. However, warfarin therapy is limited by a very narrow therapeutic window and can result in sub- or supra-therapeutic anticoagulation in 50% of patients[3]. Patient management can also be tedious. Frequent laboratory testing and follow-up is required for a good therapeutic outcome.

Several new anticoagulation agents are currently at different stages of clinical investigation.

These agents have theoretical advantages compared to conventional therapy, including:

- rapid therapeutic effect
- dependable pharmacokinetics
- limited drug interactions
- lack of need for regular blood level monitoring[2]

A closer look at DTI

Dabigatran, a DTI, offers the advantage of producing a predictable anticoagulant response without known food or drug interactions, thereby eliminating the need for coagulation monitoring. However, unlike ximelagatran — another DTI market entry rejected by the FDA — dabigatran does not appear to exhibit a significant hepatotoxic effect, with transaminase elevations seen in less than 1% of the population[3]. Dabigatran was first examined in patients with AF in the *PETRO* study. This was a Phase II randomized comparison of dabigatran with warfarin in 502 patients with AF and at least one additional risk factor for stroke. Thromboembolic and bleeding outcomes were similar between the 150 mg dose of dabigatran and warfarin[3]. Though yet to be FDA-approved, results of this study have paved the way for two other ongoing larger trials.

A closer look at FXaI

New oral factor Xa inhibitors, such as rivaroxaban and apixaban, inhibit factor Xa directly without antithrombin III mediation (as opposed to indirect FXaI such a fondaparinux and idraparinux, which have generated concerns about risks of long-term, irreversible factor Xa inhibition and the current lack of specific antidotes). Rivaroxaban is a potent FXaI administered once daily. It was shown to have predictable dose-proportional pharmacokinetics in Phase I studies and dosing was not influenced by gender and body weight[3]. However, it has potent interactions with CYP3A4 inhibitors, such as macrolides and ketoconazole. Rivoraxaban is currently under investigation as a direct comparator to warfarin in the *ROCKET-AF* study.

Apixaban is also a direct FXaI. Its mechanism of action is similar to rivoraxaban and has been evaluated in a phase II study for prevention of venous thrombosis in patients undergoing total knee replacement[3]. A composite end-point of venous

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Vision Statement

In conjunction with the Sisters of Mercy, our cardiovascular care team is dedicated to providing patients with compassionate, quality, cost-effective care through state-of-the art advancements in research, diagnostic screening, surgical and interventional procedures, clinical education and preventive/wellness programs for the improvement of cardiovascular health.

Cardiac Monitor — a resource for you

Distribution of *Cardiac Monitor* is intended for cardiologists and primary care physicians. The information included in this newsletter is provided as an educational service. Mercy respects your privacy. If you prefer not to receive any further communications from us, please send a brief note to Candice Brooks, Mercy Heart & Vascular Institute, 3939 J Street, Suite 220, Sacramento, CA 95819, and include the mailing label from this newsletter if possible. It may take up to 30 days to process your request.

CARDIOLOGY AND PRIMARY CARE

Common questions patients may ask about atrial fibrillation

Mercy Heart & Vascular Institute provides comprehensive treatment of atrial fibrillation (AF), including medication and the latest minimally invasive catheter and surgical ablation therapies. Cardiologists, cardiac electrophysiologists and cardiac surgeons work together to evaluate patients with atrial fibrillation and determine the best course of treatment. The three main goals of AF treatment are to reduce the patient's stroke risk, manage or control AF and restore a normal heart rhythm.

It is clear there is a need for further understanding of AF by many patients. More than 200 people attended a community lecture hosted by Mercy Heart & Vascular Institute in August 2008, and a question-and-answer session at the end of the lecture gave attendees the chance to ask some of the same questions primary care physicians may receive in their offices.

Following is just a small portion of the questions asked. A complete list can be found online (see box).

Q: What are the survival rates for an atrial ablation procedure?

A: Neither of the ablation procedures improve survival; their aim is to improve the quality of life. The mortality complication of each procedure is extremely low, at around 0.05%.

Q: When I asked my doctor if I had atrial fibrillation, he said I had a heart flutter. Is there a distinction?

A: Atrial flutter is different from atrial fibrillation. Catheter ablation is also used for cure of atrial flutter. The success of catheter ablation for atrial flutter is much higher than for atrial fibrillation.

Q: Are ablations recommended a second time for irregular flow of heart beat or slow beat?

A: Ablation does not help a slow heart rate. But if a patient has had a prior ablation and requires a repeat procedure to help cure atrial fibrillation, a second procedure may be feasible.

Q: Does a coronary stent or defibrillator effect atrial fibrillation and put the heart in a normal rhythm?

A: The role of a coronary stent is to keep the heart arteries open. A defibrillator treats certain abnormal rhythms that arise from the lower chambers of the heart (the ventricles). But neither play a direct role in treatment of atrial fibrillation.

Q: Is a fast or a slow heart rate more dangerous? What are the rates that are dangerous?

A: A fast or a slow heart rate during atrial fibrillation can result in different types of symptoms and problems. There are no absolute "dangerous" cut-off values, as these numbers may differ from patient to patient. But a normal heart rate should range between 60 and 100 beats per minute.

Q: How effective is a beta blocker without coumadin for atrial fibrillation in regard to having a stroke?

A: A beta-blocker plays no role in preventing stroke in atrial fibrillation. A beta-blocker only helps to keep the heart rate from going rapidly in atrial fibrillation. Coumadin is the only current therapy shown to reduce the risk of stroke in atrial fibrillation.

Q: What are the side affects of coumadin over time? Can you stay on coumadin forever?

A: The most common side effect of coumadin is excessive bleeding, particularly during surgery or traumatic accidents. But most people tolerate coumadin very well without major problems. Many patients take coumadin life-long without any bad outcomes.

A complete list of questions and answers from Mercy's A-Fib Community Lecture is available at mercygeneral.org/afib.

Medication advances help prevent stroke in atrial fibrillation

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thrombosis and all cause mortality was lower in patients treated with apixaban as compared with enoxaparin or warfarin ($p<0.01$)[3]. Moreover, major bleeding was lower in the apixaban group compared to warfarin[3].

Apixaban is also being compared to warfarin for prevention of stroke and systemic emboli in patients with non-valvular AF and at least one risk factor for stroke in the *ARISTOTLE* trial. Part of this clinical trial is being conducted through Regional Cardiology Associates with Gearoid O'Neill, MD, as Principal Investigator.

Mechanical advancements in stroke prevention

Recently, novel mechanical approaches for prevention of thromboembolic stroke have also been evaluated, including two devices for percutaneous occlusion of the left atrial appendage: *percutaneous left atrial appendage transcatheter occluder (PLAATO)* and *WATCHMAN* left atrial appendage system.

In 108 patients with a mean *CHADS*^{2} score of 2.5, who received a *PLAATO* device, the annual rate of stroke was 2.2% compared with an expected annual risk of 6.3% for this population — an estimated 65% reduction in risk[2].

The preliminary experience with the *WATCHMAN* device in 66 patients has also shown safety and feasibility[2], and a large multicenter randomized trial of the *WATCHMAN* left atrial appendage system for embolic *PROTECTion in patients with Atrial Fibrillation (PROTECT AF)* is currently ongoing.

Surgical left atrial appendage isolation using the purse string technique, neck ligation or surgical staplers via thoracoscopy, limited sternotomy or as an adjunct to open heart surgery, may also be considered for prevention or reduction of thromboembolism. A pilot study in 77 patients has demonstrated the procedure to be safe and feasible, when performed at the time of coronary bypass grafting[2]. A randomized, safety and feasibility study of the adjunct surgical closure of the appendage in 2,500 patients (*Left Atrial Appendage Occlusion Study [LAAOS]*) is currently under way.

References

1. Usman MH, Notaro LA, Patel H, Ezekowitz MD. New developments in anticoagulation for atrial fibrillation. *Curr Treat Options Cardiovasc Med* 2008;10:388–97.
2. Savelieva I, Camm J. Update on atrial fibrillation: part I. *Clin Cardiol* 2008;31:55–62.
3. Umer Usman MH, Raza S, Raza S, Ezekowitz M. Advancement in antithrombotics for stroke prevention in atrial fibrillation. *J Interv Card Electrophysiol* 2008;22:129–37.

Newsworthy

CHAMP expansion

Mercy Heart & Vascular Institute is now accepting patient referrals from Mercy Medical Center Redding for the Congestive Heart Active Management Program (CHAMP®). Physicians who refer patients will benefit from an experienced team of professionals who help patients learn to manage their heart disease after they leave the hospital. Working with the primary care physician (who remains in charge of overall care), registered nurses provide regular patient phone interaction and education with recommendations for diet changes or medication modifications. Additional team members include cardiologists, clinical pharmacists, registered dietitians and others.

Referral Resources

The following Mercy programs are available for physicians to refer their patients for help managing heart disease.

Heart Smart and CHAMP™	(916) 564-2880
Anticoagulation Clinic	(916) 733-5350
Cardiac Conditioning:	
Mercy General Hospital	(916) 453-4521
Mercy San Juan Hospital	(916) 537-5296
Smoking Cessation	(916) 453-4927
Mercy Mall Walk Program	(916) 564-2880
ICD Support Group	(916) 733-6966
Mended Hearts Support Group	(916) 453-4521

RESEARCH NEWS

Mercy Heart & Vascular Institute is participating in a national study called SATURN to determine if one of two statin medications has an effect on the percentage of atheroma in the coronary artery over a period of two years.

The SATURN trial will compare the effects of Rosuvastatin (Crestor) with the effects of Atorvastatin (Lipitor) on the percentage of atheroma, measured by intravascular ultrasound (IVUS), after two years of treatment in patients with coronary artery disease.

Eligible patients will be invited to participate if they are scheduled for an elective or urgent heart catheterization. Patients will undergo their coronary angiogram and have an IVUS during the procedure. This is used as a "baseline" exam. Once they meet all eligibility requirements, patients are randomly selected to take Crestor or Lipitor and will take the maximum recommended dose based on their lab results.

Patients are seen in clinic every three months during the follow-up period. At the end of the two-year period, they return for a follow-up IVUS to determine the percentage of plaque in the "target" coronary artery. Study medication is provided during the course of the two years, as well as during all follow-up examinations.

This study hopes to show that the benefit of a statin medication goes beyond lowering cholesterol levels and stabilization of vulnerable plaque.

Mercy Heart & Vascular Institute
1-877-9HEART9
www.CHWhealth.org/MercyHeart

Mark Your Calendar

Mark your calendar for the 2009 Cardiology & Electrophysiology Symposium, "Concepts & Controversies."

Saturday, Sept. 26, 2009
7 a.m. to 3:30 p.m.
Hyatt Regency Sacramento

2008 Cardiology Symposium

Scott Baron, MD (on left) and Michael Chang, MD (on right) welcome presenter Gregg Fonarow, MD, from UCLA Medical Center to the 2008 Cardiology Symposium held Sept. 26-27 at the Sheraton Grand Hotel in Sacramento. Dr. Fonarow is the Director of the Ahmanson-UCLA Cardiomyopathy Center, Director of UCLA's Cardiology Fellowship Program and Co-Director of UCLA's Preventative Cardiology Program. More than 160 people attended to hear the latest "Concepts & Controversies" in cardiac care.

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