

## PROFESSION

### Doctors caution on initial bleeding risk with warfarin

The benefits of the blood thinner outweigh the risks, a study author says. HHS is seeking to highlight best practices in anticoagulation management.

By KEVIN B. O'REILLY, amednews staff. Posted Dec. 10, 2012.

Rates of serious bleeding among patients taking warfarin are much higher than those found in clinical trials of the drug and are even greater during the first month of use, according to a five-year study of 125,195 seniors with atrial fibrillation.

The findings complicate an already difficult decision-making process for patients with atrial fibrillation and highlight the importance of careful management of warfarin, especially during the first month of use, experts said. Warfarin is a generic anticoagulant that is marketed under brand names such as Coumadin and Jantoven.

Compared with clinical trials for warfarin that found serious hemorrhaging rates of between 1% and 3% per year, bleeding problems are more common in real-life clinical practice, said the study, published Nov. 26 in the *Canadian Medical Assn. Journal*. In the study, the overall rate of hemorrhaging — bleeds serious enough to send patients to the hospital — was 3.8% per person, per year.

However, during the first month of treatment, the annualized hemorrhage rates were 11.8% in all patients and 16.7% among patients with higher risk of stroke.

“The clinical implications are fairly substantial,” said Tara Gomes, MHSc, a scientist at the Toronto-based Institute for Clinical Evaluative Sciences, Canada’s leading health services research institute. “Approximately 11,000 people had a serious bleed in our study and, of those, about one in five died during the hospitalization or within seven days of being discharged.”

Gomes said the stroke prevention benefits of warfarin still far outweigh the bleeding risk for patients with atrial fibrillation, but added that physicians should inform patients starting the medication of early warning signs of hemorrhaging to avoid serious harm. The warning signs of an intracranial hemorrhage include severe headache, changes in vision, dizziness and slurring of speech. Symptoms of a gastrointestinal bleed include light-headedness, vomiting blood, and black or bloody stool.

“Patients should be aware that the first 30 days are a really important time to be watching for these symptoms,” Gomes said.

Experts on anticoagulation and drug safety echoed the message.

“This is an important study that really highlights a problem, which is that the early period of anticoagulant therapy is particularly hazardous in terms of bleeding problems or recurrent thrombosis,” said Jack E. Ansell, MD, chair of the Dept. of Medicine at Lenox Hill Hospital in New York. “These are real-life numbers telling us what’s happening in the world today in Canada, and there’s no reason to think the U.S. is that different.”

#### Best practices explored

The clinical challenge, experts said, is to dose warfarin properly so that it does its job of preventing potentially deadly blood clots while avoiding thinning the blood so much that patients have serious bleeds. Adverse drug events linked to warfarin also have been documented in the U.S. A study in the Nov. 24, 2011, issue of *The New England Journal of Medicine* found that warfarin is responsible for 33,000 emergency hospitalizations of American seniors each year.

Daniel S. Budnitz, MD, MPH, lead author of the *NEJM* study, said the Canadian findings reinforce the importance of careful anticoagulation management.

“This article highlights an area, in terms of anticoagulation safety, that is a drug safety priority and seriously affects a lot of folks,” said Dr. Budnitz, director of the Medication Safety Program in the Centers for Disease Control and Prevention’s Division of Healthcare Quality Promotion.

Improving anticoagulation management is the top medication safety focus of the Dept. of Health and Human Services’ Partnership for Patients initiative, Dr. Budnitz said. The HHS is collaborating with networks of health care organizations to highlight best practices in anticoagulation management and improve care coordination.

A newer generation of blood thinners dubbed novel anticoagulants offers patients and physicians different therapeutic options. Two of them — dabigatran (Pradaxa) and rivaroxaban (Xarelto) — have already been approved by the Food and Drug Administration, and another is likely to be approved soon, said Dr. Ansell, a hematologist who specializes in thrombotic disorders and antithrombotic therapy.

“These drugs offer great advantages in that they don’t require monitoring,” he said. “The dose is a predictable one, and you give a fixed dose to all patients, generally speaking. That’s helpful in avoiding the over- or under-coagulation you see early on with warfarin. But none of these drugs is without the potential for bleeding complications. And we’ve seen over the last year or two that these newer drugs have been available that patients do bleed on them.”

---

Practicing physicians could benefit from better evidence-based guidance on which patients are best-suited to which anticoagulant, Dr. Ansell added. “There are advantages to the new drugs and advantages to the old standard, warfarin.”

In the meantime, Dr. Ansell and others said physicians starting patients on warfarin should refer them to anticoagulation clinics for follow-up monitoring and dosing adjustments or offer similar levels of weekly testing and management in their offices.

---

**ADDITIONAL INFORMATION:**

**WEBLINK**

“Rates of hemorrhage during warfarin therapy for atrial fibrillation,” *Canadian Medical Assn. Journal*, published online Nov. 26 ([www.ncbi.nlm.nih.gov/pubmed/23184840/](http://www.ncbi.nlm.nih.gov/pubmed/23184840/))

“Emergency hospitalizations for adverse drug events in older Americans,” *The New England Journal of Medicine*, Nov. 24, 2011 ([www.ncbi.nlm.nih.gov/pubmed/22111719/](http://www.ncbi.nlm.nih.gov/pubmed/22111719/))

---

Copyright 2012 American Medical Association. All rights reserved.

**RELATED CONTENT**

- » **Managing 4 risky drug types sending seniors to the ED** Oct. 1
- » **Orchestrating drug management (American College of Physicians annual scientific meeting)** May 14
- » **Quantifying adverse drug events: Med mishaps send millions back for care** June 13, 2011
- » **Rx side effects causing more hospitalizations** May 2, 2011