New drug may provide more cost-effective stroke prevention than warfarin

November 1 2010

A newly approved drug may be a cost-effective way to prevent stroke in patients with an irregular heart rhythm — and may also offer patients better health outcomes than the commonly prescribed, but potentially risky, blood thinner warfarin. That's according to a new analysis from researchers at the Stanford University School of Medicine and the Veterans Affairs Palo Alto Health Care System.

"Dabigatran is the first new drug in 20 years to be approved for stroke prevention in atrial fibrillation, and we wanted to see if it could be cost-effective even before it made its debut in the United States," said cardiac electrophysiologist Mintu Turakhia, MD, MAS, a VA investigator and an instructor of medicine at Stanford. Turakhia is senior author of the research that will appear Nov. 2 in the *Annals of Internal Medicine*.

"We found that for the average patient — 65 years and older with a risk of stroke — this drug has the potential to be a cost-effective alternative to warfarin, depending on how it is priced," said first author James Freeman, MD, MPH, a cardiology fellow at Stanford.

The researchers hope their findings will help guide decisions by physicians, insurance payers and policy-makers about the drug, dabigatran, which the U.S. Food and Drug Administration approved on Oct. 19 for the prevention of stroke in patients with atrial fibrillation. "We now have sufficient efficacy and cost-effectiveness data to help inform policy on this drug in the United States," Turakhia said.

An estimated 2.3 million Americans have atrial fibrillation, a disorder during which the heart's two upper chambers fail to beat effectively. The irregular beating can cause pools of blood to form, and if a clot escapes from the heart and blocks an artery in the brain, a stroke occurs.

Atrial fibrillation is responsible for about 15 percent of the 700,000 strokes per year in the United States. Many patients are prescribed the anticoagulant warfarin as a preventive measure. Although warfarin is effective at reducing a patient's stroke risk, it is a less-than-perfect therapy: The dosage has to be just right (too little and it could fail to prevent stroke, too much and it could lead to serious or fatal hemorrhage), and patients on the drug face constant blood testing and dose adjustment.

"Among my patients, I get asked about alternatives to warfarin a dozen times a week," said Turakhia, who specializes in the treatment and research of atrial fibrillation. "Many of them are just unhappy with the need for regular, often lifelong blood testing."

Much research has focused on developing a suitable replacement for warfarin, which has been in clinical use for 65 years. Dabigatran, an oral anti-clotting drug that requires no blood testing, emerged as one promising alternative. In a large, multicenter study published in the New England Journal of Medicine last year, the drug was about as effective as warfarin in preventing strokes but less likely to cause intracranial hemorrhages. Patients on the new drug, though, did have a slightly increased risk of heart attack.

"It looked like we may have a therapy that is at least as effective and maybe even more effective than warfarin," said Freeman. But the question remained whether dabigatran would be cost-effective. "We were very interested in answering this question," he said.

For this study, the researchers developed a mathematical model to compare outcomes and costs of warfarin, low-dose (110 mg twice daily) dabigatran and high-dose (150 mg twice daily) dabigatran. The drug isn't yet priced for the U.S. market, but the researchers used pricing from the United Kingdom, where the drug is approved for prevention of venous thromboembolism, to estimate costs of $13 per day for high-dose dabigatran. (Warfarin costs just over $1 per day.)

The team's model simulated 10,000 patients aged 65 and older with atrial fibrillation and risk factors for stroke. They determined that high-dose dabigatran prevented 1,000 more intracranial hemorrhages and 600 more strokes than warfarin was calculated to prevent, though dabigatran resulted in 400 additional heart attacks. They also determined that total lifetime costs were $143,193 for warfarin, and $168,398 for high-dose dabigatran. (Though warfarin is much less expensive than dabigatran, the costs of lifelong monitoring and adverse effects boosted its total costs.)

When taking into consideration adverse outcomes and costs, the researchers calculated that high-dose dabigatran yielded an additional 0.56 quality-adjusted-life-year — a common metric that takes into account quality of life as well as length of survival — when compared with conventional therapy with warfarin. Offering half a year of quality-adjusted life to a patient is "a fairly significant benefit," the researchers noted.

The analysis also showed that the high-dose drug came at an incremental cost over warfarin of $45,372 per quality-adjusted-life-year — well below the commonly accepted cost-effective threshold of $50,000. "That's why this is exciting," Turakhia said of the findings. Not only does the new drug "represent a breakthrough in patient convenience," but it may also make economic sense to use it, depending on how it is priced.

The researchers pointed out that their findings are dependent on the drug's price: The drug, which is marketed as Pradaxa by the Germany company Boehringer Ingelheim, would be less cost-effective if it was more expensive than the researchers' estimate. (If it were $13.70 a day, for example, its cost per quality-adjusted-life-year would exceed $50,000.) "We wanted to show what pricing range made sense," said Freeman.

In terms of study limitations, scientists and physicians are looking for ways to more efficiently determine the proper dose of warfarin, and advances in that area could also alter the comparative cost benefits. The researchers also noted that their data on efficacy came from the one large clinical trial — and that the findings needed to be validated in clinical practice. ("A lot needs to be determined outside of clinical trials, in the real world," noted Turakhia.) But "if the drug continues to perform as well as it did in studies, it could be significant competition to warfarin over the long term," said Freeman.

Provided by Stanford University Medical Center