Warfarin May Do Harm Unless Target Is Reached

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ORLANDO — Patients with atrial fibrillation who are treated with warfarin need to be in their target anticoagulation range at least 50% of the time to get a net benefit from treatment, according to a review of more than 13,000 patients.

The longer a patient stays in the target anticoagulation range the better, but when target anticoagulation is reached less than half the time a patient gets no net benefit from treatment and actually fares worse than getting no warfarin treatment at all, Dr. Alan S. Go said at the annual scientific sessions of the American Heart Association.

The standard target anticoagulant range for patients with atrial fibrillation who are treated with warfarin is an international normalized ratio (INR) of 2.0-3.0. The results from Dr. Go's analysis confirmed that this range yields the best outcomes. Additional results also showed that this INR target range is ideal for all patients, regardless of their age, even at age 80 years or older.

A warfarin regimen that keeps a patient in the INR target range less than half the time "is no better than placebo," and may actually harm patients by causing an excess of thromboembolic events or intracranial hemorrhages, said Dr. Go, assistant director for clinical research at Kaiser Permanente of Northern California in Oakland.

If patients on warfarin are having trouble staying at an INR of 2.0-3.0, the problem may be caused by the patient's diet, alcohol use, treatment with other medications that interact with warfarin, or noncompliance with the regimen, Dr. Go said in an interview. If a patient can't stay in the target range most of the time, it may be necessary to reconsider whether the patient should remain on the drug because warfarin may be causing more harm than good, he added.

Keeping patients in their target anticoagulation range more than half the time seems to depend on managing patients in an anticoagulation service that is experienced and focused on optimizing warfarin care. Kaiser Permanente of Northern California operates 21 anticoagulation clinics even though this service loses money, at least in terms of its direct costs.

When the target INR was reached 50% of the time or less, patients had an excess incidence of thromboembolic events and intracranial hemorrhages.

With this level of service, among the 13,559 patients with atrial fibrillation who were on warfarin treatment in Kaiser during July 1996–September 2003, 58% were maintained at their target INR range 60% or more of the time; 75% were kept in their target range at least 50% of the time, Dr. Go reported.

During a median follow-up of 6 years, the entire group of atrial fibrillation patients on warfarin had 1,041 thromboembolic events and 279 intracranial hemorrhages.

Analysis of data collected from these patients showed that when the target INR was reached 50% of the time or less, patients had an excess incidence of thromboembolic events and intracranial hemorrhages. When the target range was maintained 50% of the time, the rate was neutral, and among patients who maintained the target INR more than half the time, there was a direct relationship between the time spent in the target range and a reduced rate of adverse events. Patients maintained at their target INR at least 70% of the time had the lowest rate of adverse events among all patients in the study.

Additional analyses showed that all of the Kaiser atrial fibrillation patients were kept in their target INR range for an average of about 65% of the time regardless of their age, including patients younger than 60 years and those aged 80 years or older. And keeping patients at an INR of 2.0-3.0 led to reduced rates of thromboembolic events and intracranial hemorrhages, regardless of the patients' ages. In fact, because the rate of adverse events among patients who were not treated with warfarin was highest among patients aged 80 or older, the net clinical benefit from warfarin treatment maintained in the optimal INR range was greatest among patients aged 80 or older, Dr. Go said. ■