STROKE

Dabigatran and stroke prevention

Dabigatran, an orally administered direct thrombin inhibitor, has comparable efficacy to warfarin with regard to secondary stroke prevention, according to a new subgroup analysis of the Randomised Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial. In addition, dabigatran seems to carry a reduced risk of intracranial hemorrhage compared with warfarin.

“RE-LY investigated the efficacy and safety of two doses of dabigatran versus warfarin for the prevention of stroke and systemic embolism in patients with atrial fibrillation,” explains lead investigator Hans-Christoph Diener from University Hospital Essen, Germany. “Our predefined substudy looked at the 20% of patients with prior stroke and transient ischemic attack in the study.”

The RE-LY study was a prospective randomized, open-label, blinded end point (PROBE) trial, which was designed to demonstrate noninferiority of dabigatran against warfarin in terms of stroke prevention. The full study population consisted of 18,113 patients with atrial fibrillation, who were recruited from 967 centers in 44 countries.

The subgroup analysis performed by Diener and colleagues involved a total of 3,623 patients, all of whom had experienced a stroke and/or a transient ischemic attack before participating in the study. The patients had been assigned to receive warfarin ($n = 1,195$), or a twice-daily 110 mg or 150 mg dose of dabigatran ($n = 1,195$ and $n = 1,233$, respectively).

Consistent with the overall results of the trial, warfarin and the two doses of dabigatran all reduced the risk of stroke or systemic embolism to a similar degree in the subgroup analysis. Intracranial bleeding occurred significantly less frequently in the two dabigatran groups than in the warfarin group, and the 110 mg dose of dabigatran was associated with a lower risk of major bleeding than either warfarin or 150 mg dabigatran.

The investigators acknowledge several limitations of the RE-LY trial, including the PROBE design, in which the participants knew which of the two drugs they were receiving (although the dose of dabigatran was not disclosed to patients who were assigned to this drug). Also, patients who had experienced a stroke or transient ischemic attack in the 2 weeks leading up to enrollment were excluded from the trial, so the researchers were unable to establish the relative efficacies of the two drugs in the period immediately following these events.

The results of the RE-LY subgroup analysis provide evidence that dabigatran is effective for the secondary prevention of stroke in individuals with atrial fibrillation, and is likely to have a more-favorable safety profile than warfarin, especially with respect to the risk of cerebral bleeding. Unlike individuals receiving vitamin K antagonists such as warfarin, patients receiving dabigatran do not need routine coagulation monitoring.

No firm recommendations on the use of dabigatran in patients with atrial fibrillation have yet been formulated, but the choice of dose will probably depend to a large extent on an assessment of the relative risks of stroke and hemorrhage in the individual patient.

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Original article Diener, H.-C. *et al.* Dabigatran compared with warfarin in patients with atrial fibrillation and previous transient ischemic attack or stroke. *Lancet Neurol.* **9**, 1157–1163 (2010)