Letters to the Editor

The Hurdles of Warfarin and the Hurdles of Clinical Practice

To the Editor:

We have carefully read the interesting article by Hylek et al focusing on a pivotal issue in the prevention of atrial fibrillation–related stroke.1 The article explored the challenge of guidelines adherence in an elderly population with atrial fibrillation at variable hemorrhagic risk profile. Only 51% of the entire population was discharged with warfarin prescription given the presence of some contraindications for the remaining cohort. Some points, in our opinion, deserved to be more extensively discussed. Despite the widespread agreement that a “rate control” approach with prolonged anticoagulation could provide a better outcome than “rhythm control”,2 it is conceivable that part of the study population could have been eligible for electrical/pharmacological cardioversion, thus requiring a short 3- to 4-week period of anticoagulation therapy only,3 in particular those patients at first clinical episode (43%) and/or with atrial fibrillation duration ≤48 hours. The authors did not address this aspect, even if it clearly affected the choice for anticoagulation regimen: as known, the risk of bleeding complications with oral anticoagulants is higher in the first period of prescription, ie, when higher fluctuations of anticoagulation level happen, thus some physicians may have decided to avoid such risk for patients at high-risk profile prescribing alternative short-term regimens with quicker and more stable onset of action, such as aspirin.

Given the high incidence of ischemic heart disease in the older age, we wonder how many of these patients were already receiving aspirin for secondary prevention of ischemic heart disease, and how many underwent percutaneous coronary intervention in the preceding period: in such condition, the choice of starting warfarin therapy is even more difficult and without the help of clear guidelines. This issue would have been addressed aiming to further elucidate possible reasons for noncompliance with guidelines.

Another interesting issue is the alternatives to warfarin therapy. Eighteen percent of patients with contraindications for warfarin were prescribed to take 81 mg. All current guidelines agree with a unique dosage, ie, 325 mg daily, although based on the results of a single trial,5 thus, reasons to administer a lower non–evidence-based dosage remain unclear. In our opinion, also the choice to not administer an antithrombotic medication in 22% of population with contraindication to warfarin seemed worth investigation.

In conclusion, the authors cited the Sportif trials. Ximelagatran has emerged as a new and promising alternative to warfarin in virtue of its oral administration without requiring blood sampling for dose adjustments, and its predictable anticoagulant response in the absence of severe renal impairment. Some concerns over its safety profile, on the other hand, were raised quickly, and currently all marketing and developments have been stopped given a further case of fatal hepatic injury.6 Vitamin K antagonists are far from being the ideal drug, but they are certainly the best we have for stroke prevention in atrial fibrillation: the very next challenge is to find a reliable alternative, and the novel candidate aiming to replace warfarin could be another direct thrombin inhibitor, dabigatran, whose first phase III trial began enrollment in December 2005 with a planned population size of 15 000 patients.

Disclosures

None.

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