



Merry Christmas

PIC QUESTION OF THE WEEK: 12/20/10

Q: Identify some of the major characteristics of the new oral anticoagulant known as dabigatran.

A: During the past several decades, *oral* anticoagulant therapy has been synonymous with the administration of warfarin. There were few developments in this method of anticoagulation during the past fifty years; however, this recently changed upon the approval of dabigatran (Pradaxa; Boehringer-Ingelheim). This thrombin inhibitor is labeled to reduce the risk of systemic embolism and stroke in patients with non-valvular atrial fibrillation. Recommended dosage is 150 mg twice daily. Thrombin plays a significant role in the coagulation cascade by converting fibrinogen to fibrin as well as stimulating platelet aggregation. Dabigatran and its metabolites are competitive, direct thrombin inhibitors and affect both free and clot-bound thrombin. One of the distinct benefits of dabigatran over warfarin is that routine laboratory monitoring (e.g. INR) is unnecessary with the new agent. Patients should, however, have their activated partial thromboplastin time (aPTT) measured prior to undergoing surgical procedures. Another advantage of dabigatran in comparison to warfarin is the apparent lack of potential for significant drug interaction. The drug is a substrate of the efflux transporter P-glycoprotein (P-gp; *see PIC Question 9/14/09*); however, dosage adjustment does not appear necessary when combined with medications affecting P-gp such as ketoconazole, verapamil, etc. Patients should be monitored closely if they are concurrently receiving anti-platelet agents such as clopidogrel and aspirin. A recent study concluded that dabigatran was more cost-effective and increased the quality of life compared to warfarin in patients with atrial fibrillation. In addition, results from the RE-LY trial indicated that the rates of systemic embolization and stroke in patients with atrial fibrillation were also lower in the dabigatran-treated group. One negative aspect of this trial was that the rate of gastrointestinal bleeding was significantly higher (1.51%) in those receiving dabigatran versus those administered warfarin (1.02%). There appear to be several distinct advantages of dabigatran over warfarin and the drug will likely be evaluated and administered for the prophylaxis and treatment of numerous thromboembolic disorders. Hopefully, its safety profile and lack of potential for drug interaction will remain at the same level as currently recognized. This drug and several related compounds now being evaluated will undoubtedly have a significant impact on the future role of warfarin in anticoagulant therapy.

References

- Wallentin L, Yusuf S, Ezekowitz DM, et al. Efficacy and safety of dabigatran compared with warfarin at different levels of international normalized ratio control for stroke prevention in atrial fibrillation: an analysis of the RE-LY trial. 2010;376:975-83.
- New drug: Pradaxa (dabigatran). Pharmacist's Letter/Prescriber's Letter 2010;26(11):261101
- Dabigatran etexilate (Pradaxa) - a new oral anticoagulant. Med Lett Drugs Ther 2010;52:89-90
- Freeman J, Zhu R, Owens D, et al. Cost-effectiveness of dabigatran with warfarin for stroke prevention in atrial fibrillation [published online ahead of print November 1, 2010]. Ann Intern Med. PMID: 0003-4819-154-1-201101040-00289.

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