



*The Willow Tree*

## PIC QUESTION OF THE WEEK: 7/06/09

Q: Is there any relationship between the use of enteric-coated (EC) aspirin and aspirin resistance?

A: Aspirin resistance is generally described as *the failure of aspirin to produce expected pharmacologic effects including inhibition of platelet aggregation and suppression of thromboxane A<sub>2</sub> (TXA<sub>2</sub>) production*. Despite its many benefits, aspirin has some potentially significant adverse effects including gastrointestinal (GI) toxicity. Aspirin inhibits cyclooxygenase (COX) and depletes cytoprotective prostaglandins (e.g. PGE<sub>2</sub>) resulting in an increased risk of gastric ulceration and bleeding. This effect does not appear to be dose-related. To minimize GI effects, some aspirin products have been formulated with an enteric coating. Regular aspirin disintegrates in an acidic environment (i.e. the stomach) while the EC formulation is absorbed in the alkaline milieu of the small bowel. This alternative absorption site reduces the frequency of GI erosions and blood loss. On the other hand, it has been suggested that EC preparations are less bioavailable than regular aspirin. Some researchers propose that EC aspirin might provide inadequate platelet inhibition in some patients and is more likely than regular aspirin to result in reduced response. An earlier study reported the failure of EC aspirin to achieve adequate serum thromboxane B<sub>2</sub> (TXB<sub>2</sub>, the stable metabolite of TXA<sub>2</sub>) inhibition. This trial used a crossover design and compared the effectiveness of EC and plain aspirin products in healthy volunteers. The researchers evaluated three EC formulations (each 75 mg), 1 dispersible (placed in water) tablet (75 mg), and 25 mg standard release aspirin plus 200 mg modified-release dipyridamole (Aggrenox). Compared to other tested products, dispersible aspirin was superior in its effect on serum TXB<sub>2</sub> inhibition. Treatment failure (<95% inhibition of serum TXB<sub>2</sub> formation) occurred in nearly 20% of subjects receiving the non-dispersible preparations. No treatment failures occurred in those receiving dispersible aspirin. All of the products tested were considered inferior to dispersible aspirin in regard to their effect on serum TXB<sub>2</sub> levels. The three EC products tested were the least effective. In another study consisting of patients with stable cardiovascular disease, researchers examined the bioavailability and degree of platelet COX inhibition of 75 mg doses of EC aspirin. Interestingly, younger and heavier patients and those with a previous myocardial infarction were most likely to have an inadequate therapeutic response. Approximately 44% of patients failed to attain optimal serum TXB<sub>2</sub> inhibition. There is some evidence that in occasional patients EC aspirin may provide less inhibition of thromboxane production than standard preparations. Whether this subsequently results in a greater frequency of cardiovascular events has yet to be established.

### References:

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**The PIC Question of the Week is a publication of the Pharmaceutical Information Center, Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA 15282 (412.396.4600).**