

Dabigatran, fears in doctors' minds.

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Dear Editor,

The fact that many doctors still refuse to replace the anticoagulant warfarin with dabigatran, despite dabigatran's better safety profile, is not a scientific problem but a psychological one. In my view there are four fears in doctors' minds:

- 1) Fear of dabigatran's hidden higher incidence of bleeding.
- 2) Fear of bleeding crisis when dabigatran's antidote is not available.
- 3) Fear of overdose in Thai population when extrapolating the dose from Caucasian population.
- 4) Fear of higher cost for patients.

I address these four fears one by one below.

Fear of dabigatran's hidden higher incidence of bleeding, is a fear based on news rather than evidence, particularly the high number of law suits reported on the internet. Some lawyers have launched websites offering their services to lodge suits against dabigatran without any of the usual upfront payments. The FDA itself used to issue warning letters to say that it has been working on post marketing reports of dabigatran in view of the detection of hidden bleeding incidence not identified in premarketing research. Some governmental health agencies in countries such as Australia and Japan have also issued warnings on the uncertainty of the bleeding incidence rates of dabigatran. But news is only news and for the most part anecdotal. There has not been, to date, any reliable evidence showing that dabigatran carries a higher incidence of bleeding than warfarin does. On the contrary, the evidence shows that dabigatran carries lower overall bleeding incidence. Data from RE-LY study which is the biggest study of its kind indicates that dabigatran has lower bleeding incidence than warfarin. Clinical practice guidelines such as the European Society of Cardiology (ESC) advise the use of dabigatran as a treatment of first choice for prevention of stroke in AF since 2012. So rest assured, news goes off in one direction but the evidence goes in another.

Fear of a bleeding crisis without there being an antidote should be alleviated because there is an antidote to dabigatran now. A study using the dabigatran antidote called Idarucizumab was recently published in the New England Journal of Medicine. It is a cohort study of 503 dabigatran users, of whom 301 users belong to the bleeding complication group and 202 users belong to preparation for operation group. The antidote idarucizumab, 5 grams dose was injected intravenously then the coagulograms were follow within 4 hours. The study shows that idarucizumab can reverse the anticoagulation effect of dabigatran by 100%. The peak reversal time is 2.5 hours for the bleeding complication group and 1.6 hours for preparation for operation group.

Fear of Caucasian dose in Asian patients should be allayed given the study done in Japan. In that study researchers compared the dose of 150 mg vs 110 mg in Japanese patients and found that the dose of 150 mg can achieve better stroke prevention than the dose of 110 mg.

Fear of the cost of treatment, should be resolved by presenting the medication as an option to the patient. The patient should be the one to decide whether he/she will pay more or not.

In summary, up until today evidence supports replacing warfarin with dabigatran in view of the better outcomes and safety profile. Fear no more, doctor!

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