

# Trauma patients on dabigatran prompt call for "pragmatic" trials, trauma surveillance

NOVEMBER 24, 2011 Shelley Wood

**Boston, MA** - Very little can be done for a patient taking dabigatran (Pradaxa, Boehringer Ingelheim) who suffers a traumatic injury, and this new, potentially catastrophic predicament—less of an issue in the warfarin era—underscores the need for routine surveillance of new oral anticoagulants to include hemorrhagic complications and trauma deaths.

So say two trauma surgeons and an emergency room physician who authored a research letter appearing in the November 24, 2011 *New England Journal of Medicine*. They write that they've recently cared for several patients taking dabigatran at the time of their injury, all of whom died [1].

First author on the letter **Dr Bryan A Cotton** (Center for Translational Injury Research, Houston, TX) spoke with [heartwire](#) late Friday, saying he knows that his views, as a trauma surgeon, "are a little bit skewed."

"We don't see anything *but* complications with these patients, we don't see the people with wonderful interactions with dabigatran. All we see is the bad, but when you do, it's a horrible feeling."

Cotton says "you kind of roll your eyes when you hear that an [incoming trauma] patient is on Coumadin, thinking 'this is going to increase their risk,' but at least you know there are some things you can do. . . . Now, with dabigatran, if I hear a patient is on Pradaxa, I get chest pain myself when I hear it. All of us do."

Cotton and colleagues point out that trauma is the fourth-leading cause of death in the US, reaching 40 000 deaths per year among men and women over age 65. While hemorrhagic complications can also be catastrophic in people taking warfarin, patients on the older drug have the edge over those taking newer oral anticoagulants in a number of ways.

First, the degree of warfarin anticoagulation can be easily assessed, whereas no such tests exist for dabigatran. Second, there are strategies to rapidly reverse the anticoagulant effect of warfarin using vitamin K, plasma factor VIIa, and factor concentrates, Cotton et al note. By contrast, coagulopathy is mostly "irreversible" in patients taking dabigatran.

"Currently, the only reversal option for dabigatran is emergency dialysis (as suggested in a single line in the package insert)," Cotton et al write. "The ability to perform rapid dialysis in patients with bleeding whose condition is unstable or in those with large intracranial hemorrhages will present an incredible challenge, even at level one trauma centers."

Among patients taking dabigatran seen by Cotton et al, all appeared to have normal coagulation on conventional tests, but were grossly abnormal using rapid thromboelastography (rTEG). One patient who suffered a fall and developed neurological deficits died shortly after emergency craniotomy. "Unfortunately, even with the aid of rTEG, supportive care is all that is available in the emergency setting," they write.

In their letter, Cotton and colleagues urge the FDA to consider the "generalizability" of study findings for new, upcoming oral anticoagulants, and to require more pragmatic trials. "We strongly urge that hemorrhagic complications and death resulting from trauma be included as part of the routine surveillance of all newly approved oral anticoagulants," they conclude.

Cotton said he in no way expects the RE-LY investigators to go back and redo their trial, but he believes real-world trauma events should be captured in trials of other anticoagulants that are still ongoing. He also wants trauma deaths, which are not typically captured in postmarketing surveillance, to be included.

In fact, Cotton says he was surprised and pleased to get a call from Boehringer-Ingelheim after his letter was published, asking for details on the three patients, suggesting they are "taking this very seriously." They also told him that the company is actively working on an antidote to reverse dabigatran's effects.

"But until I have that in my back pocket, this is a bad problem," Cotton said, although he acknowledged a traumatic injury, itself, represents a "small risk."

Cotton hopes his letter will spur physicians to discuss the risks in the case of trauma with their patients as part of the discussion of whether to start the drug in the first place or switch from warfarin—something he thinks is not happening enough. "The harm when this happens is real and irreversible, and there ought to be a more balanced discussion between patients and physicians."