Renal risk stratification with the new oral anticoagulants

(JULY 2013)

TO THE EDITOR: I read with interest the review of the new oral anticoagulants by Fawole et al[1] and agree with their comments on the prevention of bleeding and the importance of monitoring renal function in managing patients on the new classes of oral anticoagulants. However, no specifics were given on how to proceed. Thus, I recommend that renal risk stratification be done before and 1 week after starting these new drugs.

Originally, the US Food and Drug Administration approved dabigatran (Pradaxa) at a dose of 150 mg orally twice daily in patients with a creatinine clearance of 15 to 30 mL/min/1.73 m^2. This dosing corresponded to the estimated glomerular filtration rate (eGFR) in patients with stage 4 chronic kidney disease, but this dosing is contraindicated in other guidelines worldwide (Canada, Europe, the United Kingdom, Japan, Australia, and New Zealand).[2] Not unexpectedly, 3,781 serious adverse effects were noted in the 2011 US postmarketing experience with dabigatran. These included death (542 cases), hemorrhage (2,367 cases), acute renal failure (291 cases), stroke (644 cases), and suspected liver failure (15 cases).[3] Thirteen months after dabigatran's approval in the United States, Boehringer Ingelheim changed the dosage and product guidelines.[2–4] The new dosage[4] is 75 mg twice daily for patients with a creatinine clearance of 15 to 30 mL/min/1.73 m^2.

Therefore, I suggest a nephrologic "way out"[5] when using the new oral anticoagulants to avoid the problems with dabigatran noted above.

First, if these drugs are to be used in nonvalvular atrial fibrillation, risk factors should be determined using the CHADS2 or the CHADS2-VASc score. Special attention should be given to patients age 75 and older, women, and patients with a history of stroke, transient ischemic attack, or systemic embolism. All of these have been noted to be major risk factors.[6,7]

TABLE 1

Suggested dabigatran dosage adjustment according to renal function

Stage of CKD	eGFR (mL/min/1.73 m^2)	Description	Dabigatran dose
1	≥ 90	Renal injury without decreased GFR	150 mg twice daily
2	60–89	Mildly decreased eGFR	150 mg twice daily
3	30–59	Moderately decreased eGFR	150 mg twice daily
4	15–29	Severely decreased eGFR	75 mg twice daily
5	≤ 15	Renal failure	Not indicated

CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate

Second, renal risk stratification[8] should be done using a comprehensive metabolic panel before and 1 week after starting new oral anticoagulants, or if there is a change in the patient's clinical condition. Most US laboratories now provide an eGFR and the stage of chronic kidney disease.[3,5] For example (TABLE 1), if dabigatran is used, one should follow current dosing guidelines for chronic kidney disease stages 1 through 3, ie, 150 mg twice daily. If stage 4 chronic kidney disease is detected (creatinine clearance 15–29 mL/min/1.73 m^2), the updated recommended dosage is 75 mg twice daily. If stage 5 is noted (eGFR ≤ 15 mL/min/1.73 m^2), dabigatran is not indicated. Similar steps can be done using current guidelines for the other new oral anticoagulants.

This simple renal risk stratification guideline should help avoid some of the problems noted in the dabigatran postmarketing experience, which were aggravated by the lack of approval of a 110-mg dose and by misleading advertising, claiming that no blood monitoring was required.[2–5] Thus, the new oral anticoagulants should be a welcome addi-

tion to our armamentarium in patients who need them, and we hope to avoid the risks, morbidity, mortality, and expense of trying to reverse adverse effects.

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doi:10.3949/ccjm.80c.11001

IN REPLY: We agree with the comments of Dr. Pazmiño regarding specifics of renal risk stratification in patients taking the new oral anticoagulants. In order to reduce the bleeding risks associated with these agents, they should be prescribed on the basis of the individual patient's clinical characteristics. We did not discuss this since the focus of our article was management of bleeding that resulted from use of these drugs. We appreciate the recommendations of Dr. Pazmiño.

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doi:10.3949/ccjm.80c.11002

Not all joint pain is arthritis

(MAY 2013)

TO THE EDITOR: I was somewhat confused by the Clinical Picture case in the May 2013 issue.[1] The caption for **FIGURE 1** stated that the MRI showed erosions and marrow edema, which were "asymmetrical compared with the other wrist, a finding highly suggestive of rheumatoid arthritis." However, rheumatoid arthritis is generally considered to be symmetrical.[2] Was this a typographical error, or did I miss a crucial concept somewhere?

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doi:10.3949/ccjm.80c.11003

IN REPLY: We apologize for the confusion. We wanted to convey that, in that patient at that time, synovitis with erosions and edema indicating inflammation (greater on the right than on the left left) was suggestive of rheumatoid arthritis despite the asymmetry seen (findings greater in the right wrist than in the left). Given the patient's clinical findings at that time and the above imaging findings, the initial diagnosis of rheumatoid arthritis was correct. But since the patient was not responding to therapy and since the abdominal pain was worsening, we probed further. Subsequently, the patient was diagnosed with Whipple disease. The fact that inflammatory arthritis can occur in other conditions that are not rheumatologic is a primary reason we found this case worth sharing.

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doi:10.3949/ccjm.80c.11004