COX-2 selective NSAIDS

(MAY 1999)

TO THE EDITOR: Reading Dr. Mandell's article on "COX-2 Inhibitors: Promises and Concerns,"[1] it occurred to me that since COX-2-selective NSAIDs will offer no cardiovascular protective activity and can't replace low-dose aspirin, that if a substantial portion of a coronary artery disease at-risk population took them we might lose the population effect of reducing cardiovascular events. Of course, this would presume that their use becomes widespread. If this did ultimately happen many chronically ill patients with multiple comorbidities would be taking these selective agents. Unless their physician prescribed low-dose aspirin (ie, recognizing a possibly occult vascular problem) they would remain without the advantage of platelet aggregation inhibition.

In a further scenario, if the COX-2 inhibitors become even more accepted—eventually being sold over-the-counter—a larger at-risk population which currently may never see a doctor but may take over-the-counter NSAIDs will lose the platelet aggregation inhibition effect. This could lead to an increase in cardiovascular events on a population basis. Should this not be included as an additional concern?

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REFERENCES

1. Mandell BF. COX-2-selective NSAIDs: Biology, promises, and concerns. Cleve Clin J Med 1999; 66:285–292.

IN REPLY: Dr. Ryan emphasizes, as noted in my review of the COX-2 inhibitors, that selective COX-1-sparing drugs will not inhibit platelet function, and, therefore, presumably will have no cardiovascular protective effect. It is incumbent upon physicians to recognize that aspirin likely has value in protecting patients from myocardial infarction above and beyond that offered by the reversible, nonselective NSAIDs currently available, and certainly would be expected to be more effective than the new selective NSAIDs. The use of selective COX-1-sparing agents concurrently with aspirin will hopefully not diminish aspirin's efficacy in protecting patients from platelet-dependent thrombotic events. Physicians should continue to counsel patients regarding the use of aspirin, balancing the potential of bleeding complications against cardiovascular risk protection. Use of aspirin should not be a decision left solely to the patient.

Whether intermittent use of NSAIDs has any value to protect patients from "occult vascular problems" is not evident. If these patients are switched to COX-2 selective therapy, additional low-dose aspirin should be considered if they are at risk for cardiac disease. With this strategy, however, there may be some increased risk of gastric toxicity due to the aspirin, above that of the selective NSAIDs alone.

Update on COX-2 inhibitors

Additional issues that have arisen since publication of this review include the release of a second COX-1-sparing, COX-2 selective NSAID. Rofecoxib (Vioxx) has been approved for treatment of the pain and symptoms of osteoarthritis, as well as for the treatment of acute pain and dysmenorrhea. Rofecoxib is dosed once-daily from 12.5 to 25 mg. Rofecoxib, like celecoxib (Celebrex), should at present be used with caution in patients with renal or hepatic insufficiency or aspirin-sensitive bronchospasm. It has been ascribed with development of peripheral edema, particularly at the higher doses.

There has been a change in the labeling of celecoxib, indicating that there is a potential interaction between this drug and warfarin. Some patients who have been using either rofecoxib or celecoxib concurrently with warfarin have experienced a variable increase in their international normalized ratio (INR). Some patients have experienced clinical bleeding. This is likely of greatest significance in patients maintained at a high therapeutic INR. As with the addition of all medications, the INR should be regularly rechecked in patients taking warfarin.

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Hypertension in the elderly

(SEPTEMBER 1999)

TO THE EDITOR: I am addressing this letter in regards to Dr. Wilbert Aronow's article: "Hypertension in elderly patients: Treatment reduces mortality, but is underused."[1] First of all, this is another excellent article which I enjoyed reading.

However I found it interesting that, in light of the United Kingdom Prospective Diabetes Study (UKPDS) trial,[2] Dr. Aronow recommends an angiotensin receptor blocker (ARB) if an angiotensin-coverting enzyme (ACE) inhibitor fails in diabetic patients. The UKPDS trial examined the efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type-2 diabetic patients. They found, "Blood pressure lowering with captopril or atenolol was similarly effective in reducing the incidence of diabetic complications." The endpoints included death, all-cause mortality, and surrogate measures of micro-and macrovascular disease. There was no increase in hypoglycemic attacks.

Thanks again for this journal!

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REFERENCES

1. **Aronow WS.** Hypertension in elderly patients: Treatment reduces mortality, but is underused. Cleve Clin J Med 1999; 66:487–493
2. **UK Prospective Diabetes Study Group.** Efficacy of atenolol and captopril in reducing the risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. BMJ 1998; 317:713–720.

IN REPLY: The results of the UKPDS trial are difficult to interpret, since many of the patients ended up being treated with more than one antihypertensive drug. The patients enrolled in the study had early type-2 diabetes mellitus and were at lower risk for developing microalbuminuria and proteinuria than would be patients with diabetes mellitus of a longer duration.

The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI) states that ACE inhibitors are preferred in patients with hypertension and diabetic nephropathy.[1] "If ACE inhibitors are contraindicated or not well tolerated, angiotensin II receptor blockers may be considered."[1]

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1. **1997 Joint National Committee.** The sixth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI). Arch Intern Med 1997; 157:2413-2444.

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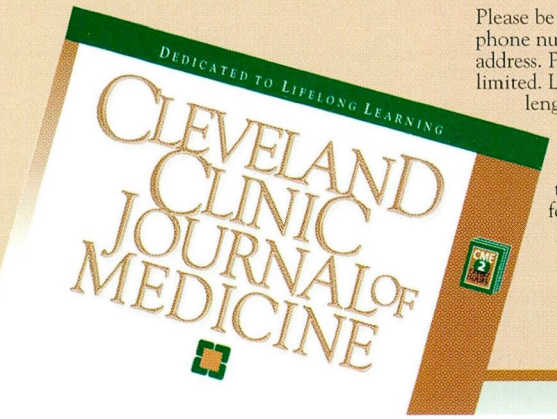

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