

Clinical Update

COX-2 inhibitors and renal function in elderly people

Swan SK, Rudy DW, Lasseter KC, Ryan CF, Buechel KL, Lambrecht LJ, et al. Effect of cyclooxygenase-2 inhibition on renal function in elderly persons receiving a low-salt diet: a randomized, controlled trial. *Ann Intern Med* 2000; 133:1-9.

Background

About 10 million prescriptions for NSAIDs are dispensed yearly in Canada.¹ NSAIDs exert their effects through the inhibition of cyclo-oxygenase (COX), an enzyme that catalyses the synthesis of prostaglandins. Two isoforms of COX (COX-1 and COX-2) have been identified. Traditional NSAIDs inhibit both of them, whereas the newer COX-2 inhibitors selectively inhibit COX-2. Although renal failure can occur with traditional NSAIDs, it is unclear whether this risk can be avoided with the use of COX-2 inhibitors.

Question

Does rofecoxib, a COX-2 inhibitor, impair renal function in elderly people?

Design

This randomized, double-blind, placebo-controlled trial enrolled elderly people aged 65–80 years.² Numerous exclusion criteria applied; all subjects were in good general health and took no medications that might impair renal function. Subjects were randomly

assigned to receive a 5-day course of one of the following treatments: rofecoxib, 12.5 mg/d; rofecoxib, 25 mg/d; indomethacin, 50 mg 3 times daily; or placebo. All subjects were placed on a low-sodium diet 8 days before randomization. The primary end point was the glomerular filtration rate (GFR), calculated by measuring iodine-125-iodothalamate clearance before and after treatment.

Results

Sixty subjects (15 in each treatment arm) completed the study. The mean age was 72 years. Compared with placebo, multiple doses of rofecoxib 12.5 mg/d, rofecoxib 25 mg/d and indomethacin 150 mg/d decreased the GFR by a mean of 0.14 mL/s ($p = 0.019$), 0.13 mL/s ($p = 0.029$) and 0.10 mL/s ($p = 0.086$) respectively. The reductions in GFR were comparable between the rofecoxib and indomethacin groups.

Commentary

This study found that rofecoxib impaired renal function among the elderly subjects as much as a traditional NSAID. The results are likely generalizable to other COX-2 inhibitors, given similar findings with celecoxib.³ Whether the results can be generalized to younger patients is unknown. The low-sodium diet, which mimics a state of decreased circulating volume, may have exaggerated the observed re-

duction in GFR. Conversely, the exclusive use of healthy subjects and the short duration of drug exposure may have underestimated the usual risk among elderly patients. Of note, this study did not look for other renal complications of NSAIDs, such as interstitial nephritis.

Practice implications

Like traditional NSAIDs, selective COX-2 inhibitors can impair renal function. These drugs, therefore, should be used with caution in elderly patients, in patients with renal insufficiency and in patients with decreased circulating volume because of diuretic use, congestive heart failure or cirrhosis. — *Benjamin H. Chen*

The Clinical Update section is edited by Dr. Donald Farquhar, head of the Division of Internal Medicine, Queen's University, Kingston, Ont. The updates are written by members of the division.

References

1. Tambllyn R, Berkson L, Dauphinee D, Gayton D, Grad R, Huang A, et al. Unnecessary prescribing of NSAIDs and the management of NSAID-related gastropathy in medical practice. *Ann Intern Med* 1997;127:429-38.
2. Swan SK, Rudy DW, Lasseter KC, Ryan CF, Buechel KL, Lambrecht LJ, et al. Effect of cyclooxygenase-2 inhibition on renal function in elderly persons receiving a low-salt diet: a randomized, controlled trial. *Ann Intern Med* 2000; 133:1-9.
3. Rossat J, Maillard M, Nussberger J, Brunner HR, Burnier M. Renal effects of selective cyclooxygenase-2 inhibition in normotensive salt-depleted subjects. *Clin Pharmacol Ther* 1999;66: 76-84.