

# NSAIDs Ineffective for Postop Pericardial Effusion

BY BRUCE JANCIN

ORLANDO — Diclofenac, widely prescribed to reduce pericardial effusion volume and prevent tamponade following cardiac surgery, proved ineffective in a double-blind randomized trial.

"NSAID administration seems to be useless in this setting," said Dr. Philippe Meurin, who presented the findings of the Nonsteroidal Anti-Inflammatory Treatment for Postoperative Pericardial Effusion (POPE) study at the annual scientific sessions of the American Heart Association.

The use of NSAIDs to treat postoperative persistent pericardial effusions is "an old habit" never previously examined in a clinical trial, he said. It's a popular practice: Studies indicate NSAIDs



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are prescribed in one-half to three-quarters of patients with persistent moderate to large pericardial effusions, according to Dr. Meurin of the Cardiac Rehabilitation Center, Villeneuve Saint Denis, France.

Yet there are safety concerns. NSAID therapy is associated with up to a twofold increased risk of MI, a threefold increase in renal failure, and a fourfold greater risk of GI bleeding. The risk of renal failure climbs to sixfold with concomitant ACE inhibitor therapy, and the GI bleeding risk jumps to eightfold with concomitant low-dose aspirin, he added.

POPE was a multicenter study involving 196 patients with grade 2 or greater pericardial effusion on day 15 after cardiac surgery who were randomized in a double-blind fashion to 2 weeks of diclofenac at 50 mg b.i.d. or placebo. Grade 2 is a loculated pericardial effusion of at least 10-14 mm or a circumferential one of up to 9 mm on echocardiography.

Patients with at least a grade 2 pericardial effusion constituted 3.6% of the more than 5,000 cardiac surgery patients who underwent postoperative screening echocardiography, underscoring that this potentially serious complication is uncommon.

The primary study end point was change in mean effusion grade based on fluid volume assessed echocardiographically after 2 weeks of therapy. The diclofenac group had a mean 1.36-grade decrease, not significantly different from the 1.08-grade drop in controls.

Late tamponade requiring pericardial drainage occurred in 11.2% of the placebo group, similar to the 9.2% rate in the NSAID group.

Discussant Dr. Elliott M. Antman expressed "a mixture of disappointment

and relief" at the POPE results.

He felt disappointment because persistent pericardial effusion is a potentially serious problem for which it appears there is as yet no good therapy, he said. By the time it converts into tamponade—as occurred at a 10% rate in POPE—the patient has typically been discharged from the hospital, making prompt detection of this life-threatening condition problematic.

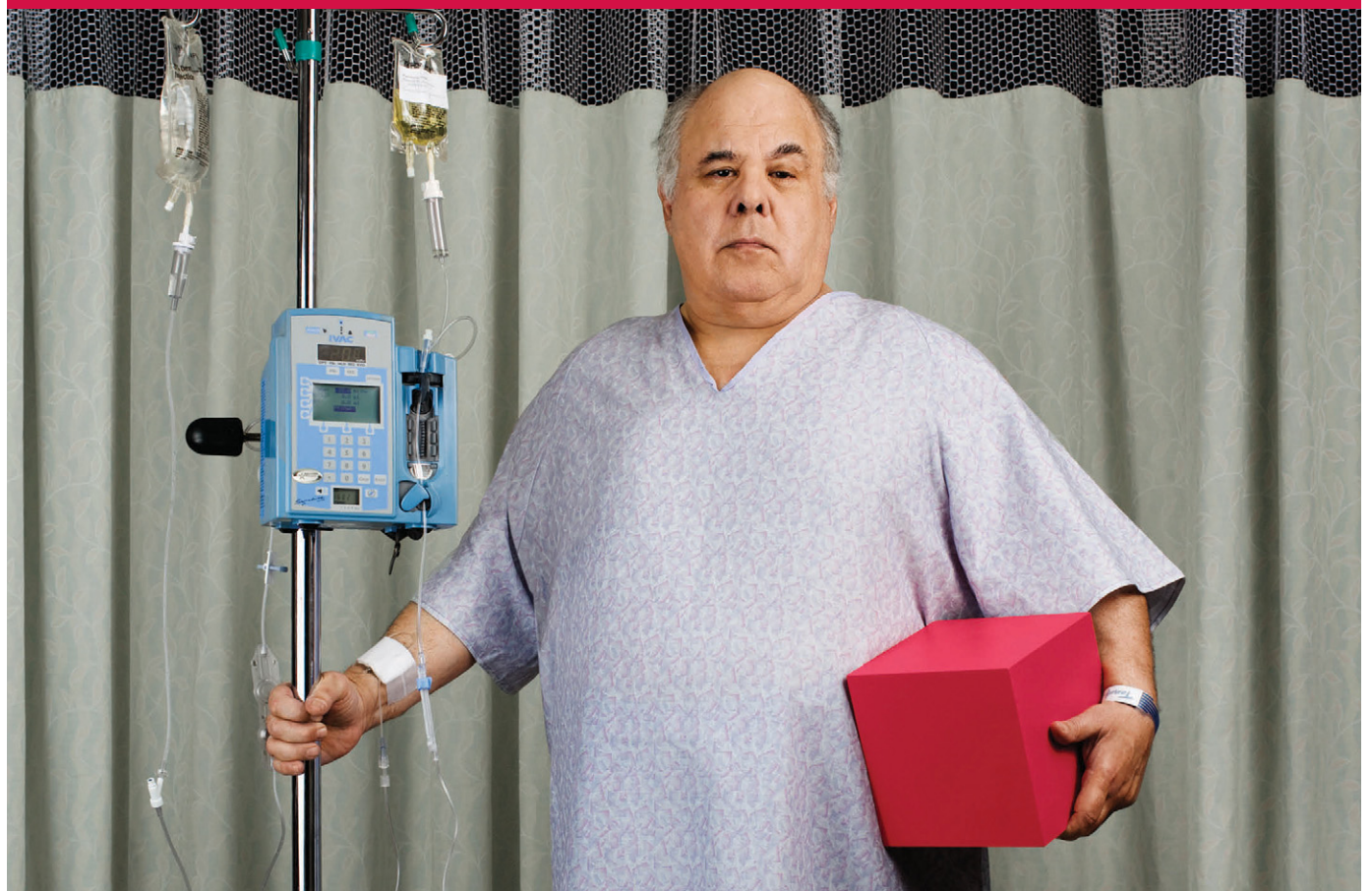
Dr. Antman said he felt relief because if POPE had shown efficacy for diclofenac it would have created a problem in light of the American Heart Association's March 2007 scientific statement advising physicians that NSAIDs are not recommended in patients who have ischemic heart disease or are at risk for it.

Diclofenac is a cyclooxygenase-2-selective NSAID and therefore poses a

greater cardiovascular risk than do non-COX-2-selective NSAIDs. "It would be on the list of drugs that I'd be a little bit more worried about in a patient who had coronary artery disease," noted Dr. Antman, professor of medicine at Harvard Medical School, Boston.

The POPE study was funded primarily by the French Society of Cardiology. Dr. Meurin reported having no relevant financial relationships. ■

## IN THE TREATMENT OF MRSA BACTEREMIA AND MRSA COMPLICATED SKIN INFECTIONS



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### INDICATIONS AND IMPORTANT SAFETY INFORMATION

CUBICIN is indicated for the following infections: Complicated skin and skin structure infections caused by susceptible isolates of the following Gram-positive microorganisms: *S. aureus* (including methicillin-resistant isolates), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae* subspecies *equisimilis*, and *Enterococcus faecalis* (vancomycin-susceptible isolates only). Combination therapy may be clinically indicated if the documented or presumed pathogens include Gram-negative or anaerobic organisms.

*S. aureus* bloodstream infections (bacteremia), including those with right-sided infective endocarditis, caused by methicillin-susceptible and methicillin-resistant isolates. Combination therapy may be clinically indicated if the documented or presumed pathogens include Gram-negative or anaerobic organisms.

The efficacy of CUBICIN in patients with left-sided infective endocarditis due to *S. aureus* has not been demonstrated. The clinical trial of CUBICIN in patients with *S. aureus* bloodstream infections included limited data from patients with left-sided infective endocarditis; outcomes in these patients were poor. CUBICIN has not been studied in patients with prosthetic valve endocarditis or meningitis.

Patients with persisting or relapsing *S. aureus* infection or poor clinical response should have repeat blood cultures. If a culture is positive for

*S. aureus*, MIC susceptibility testing of the isolate should be performed using a standardized procedure, as well as diagnostic evaluation to rule out sequestered foci of infection. Appropriate surgical intervention (eg, debridement, removal of prosthetic devices, valve replacement surgery) and/or consideration of a change in antibiotic regimen may be required. CUBICIN is not indicated for the treatment of pneumonia.

*Clostridium difficile*-associated diarrhea (CDAD) has been reported with the use of nearly all antibacterial agents, including CUBICIN, and may range in severity from mild diarrhea to fatal colitis. CDAD has been reported to occur over 2 months post-antibiotic treatment. If CDAD is suspected, antibiotic treatment may need to be suspended.

Patients receiving CUBICIN should be monitored for the development of muscle pain or weakness, particularly of the distal extremities. In patients who receive CUBICIN, creatine phosphokinase (CPK) levels should be monitored weekly, and more frequently in patients who received recent prior or concomitant therapy with an HMG-CoA reductase inhibitor. In patients with renal insufficiency, both renal function and CPK should be monitored more frequently. Patients who demonstrate unexplained elevations in CPK while receiving CUBICIN should be monitored more frequently. CUBICIN should be discontinued in patients with unexplained signs and symptoms of myopathy in conjunction with CPK elevation >1000 U/L (~5X ULN), or in patients without reported symptoms who have marked elevations in CPK >2000 U/L (≥10X ULN).

Most adverse events reported in CUBICIN clinical trials were mild to moderate in intensity. The most common CUBICIN adverse events were anemia, constipation, diarrhea, nausea, vomiting, injection-site reactions, and headache.

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