# Drug Monitor

ONLINE EDITION

## NSAIDs Effective In Reducing Pericardial Effusions?

According to several surveys, nonsteroidal anti-inflammatory drugs (NSAIDs) are prescribed to treat late postoperative pericardial effusions in up to 77% of patients. No study has ever shown their efficacy, however. Researchers from the French Society of Cardiology conducted a multicenter, prospective, double-blind, randomized, controlled study comparing the efficacy of diclofenac and placebo and found the NSAID did not have a significant effect on the size of moderate to severe pericardial effusions.

In a previous study, the researchers found that the most powerful predictor of late cardiac tamponade was the size of the effusion. During follow-up, the patients with no effusion or a small effusion did not experience late cardiac tamponade, but tamponade did develop in 11% of patients with larger pericardial effusions. Therefore, in this study, researchers studied 196 patients who had pericardial effusions grade 2 or larger (loculated effusion larger than 10 mm or a circumferential effusion of any size) seven to 30 days after cardiac surgery. Ninety-eight patients were assigned randomly to receive diclofenac 100 mg/day and 98 patients received placebo.

Transthoracic echocardiography and laboratory tests conducted 14 days after the initiation of treatment found the mean change in effusion grade was –1.08 grades for the placebo group and –1.36 grades for the diclofenac group ($P = .11$). Furthermore, a similar percentage of patients in both groups had a grade decrease of one or more (74.4% in the placebo group versus 72.4% in the diclofenac group, $P = .845$). Diclofenac also did not seem to have much effect on the frequency of tamponade (11.2% in the placebo group versus 9.2% in the diclofenac group, $P = .49$).

In conclusion, diclofenac did not significantly reduce the size of pericardial effusions or the risk of late cardiac tamponade, say the researchers. Moreover, the study confirmed that moderate to large pericardial effusion (grade 2, 3, or 4) occurring seven to 30 days after cardiac surgery is a severe condition: 10% of patients required surgical pericardiocentesis in the 14 days after they enrolled in the study.

It would seem logical that diclofenac is no more effective than placebo if inflammation is not the predominant mechanism for most postoperative pericardial effusions, the researchers say. "Furthermore, the ineffectiveness of diclofenac therapy for patients with a C-reactive protein level of at least 285.6 nmol/L suggests that no noninvasive test can separate inflammatory and hemorrhagic effusions." Therefore, they suggest that NSAIDs should not be prescribed to treat asymptomatic postoperative pericardial effusions because the minor beneficial effects of the drug do not outweigh the risks.

Source: *Ann Intern Med.* 2010;152(3):137–143.

## Better Treatment Needed for Pulmonary Arterial Hypertension

Although seven therapies have been approved to treat pulmonary arterial hypertension (PAH), their clinical effectiveness in reducing mortality remains undefined, say researchers from Consorzio Mario Negri Sud, Santa Maria Imbaro, Chieti, Italy; GVM Hospitals of Care and Research, Cotignola, RA, Italy; and University of Chicago, IL. Their findings from a previous metaanalysis showed the seven therapies had little effect on hemodynamics and no effect on survival. Since that last review, 10 new clinical trials have added data on approximately 1,500 patients. The researchers say the pooled effect of all treatments now reveals a striking mortality reduction of 39%.

Included in the analysis were 26 trials published from January 1985 to April 2009 that addressed the effects of epoprostenol (EPO), prostacyclin analogues (PCA), endothelin receptor antagonists, and phosphodiesterase-type-5 inhibitors in patients with PAH. Exercise capacity was the primary end point in most of the trials; all treatments produced a small but significant increase in capacity. All treatment options produced a mean decrease in pulmonary artery pressure (PAP) of –2.87 mm Hg ($P < .001$); EPO appeared to have a greater effect on lowering PAP than PCA or any other therapy. Although the pooled effect of all therapies was a reduction of 39% in all-cause mortality, when considering the cumulative effects within each drug family, no class of drug produced a significant reduction.

Having more than 3,500 patients in the metaanalysis allowed the researchers to explore which types of patients or therapies were responsible for these findings: For example, in trials that recruited patients with severe symptoms or advanced disease, treatment with any of the vasodilators significantly reduced mortality rates. However, "the mechanism by which mortality was reduced remains a question," the researchers say, "because it was unrelated to a specific class of drug, the dose of the drug, or the

effects of the drug on six-minute walk or hemodynamics."

These results mandate a change in thinking about the long-term use of vasodilators as therapy for patients with PAH who are nonvasoreactive—which may be "counterintuitive," the researchers admit. They also question the ethics of conducting more clinical trials that use similar designs and end points. They suggest lengthening trials to at least one year (since PAH is a fatal disease) and including new surrogate end points, such as imaging studies and biomarkers, so that future trials can better investigate the mechanisms by which treatments affect the underlying disease.

Source: *Am Heart J.* 2010;159(2):245–257. doi:10.1016/j.ahj.2009.11.028.