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Letters

Colchicine for Post-Operative Pericardial Effusion

Preliminary Results of the POPE-2 Study

The incidence of pericardial effusion is high after cardiac surgery. It peaks at the end of the first post-operative week and usually decreases spontaneously. Tamponade occurs in 1% to 2% of patients. Early tamponade (occurring during the first 7 post-operative days) is due to surgical bleeding. However, most tamponade cases occur more than 7 days after surgery (1) and may develop slowly without clear-cut clinical signs in asymptomatic patients. This situation is disconcerting because patients often have been discharged from the hospital by this time.

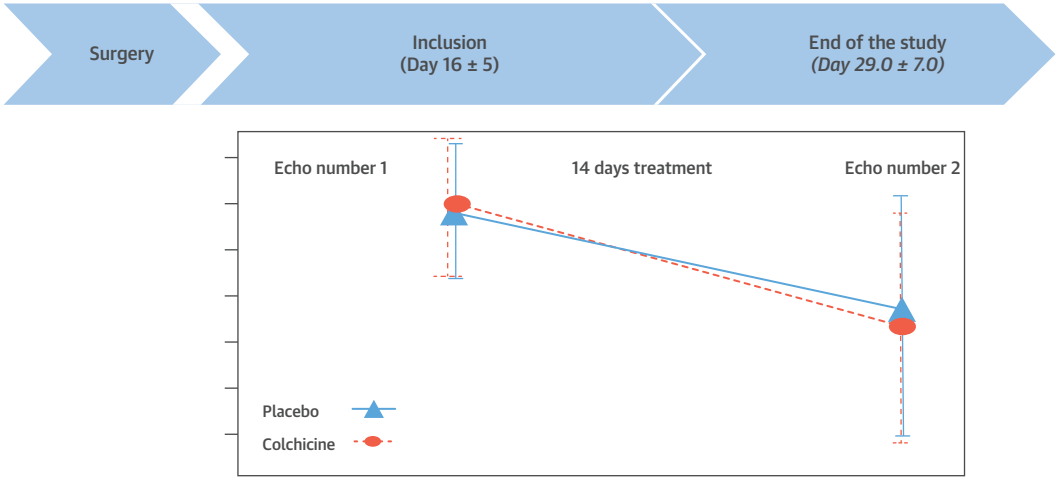
Traditionally, inflammation is considered to be involved in these late post-operative pericardial effusion events, even though a randomized study (2) showed that nonsteroidal anti-inflammatory drugs were not effective for post-operative pericardial effusions persisting >7 days after surgery and preventing late cardiac tamponade. Colchicine is an anti-inflammatory drug that is effective in treating acute pericarditis (3). Furthermore, if colchicine is administered before or within 3 days after surgery, it helps prevent post-pericardiotomy syndrome, an inflammatory post-injury pericardial syndrome that usually mimics acute pericarditis, which often involves a small pericardial effusion and with an evolution that is usually spontaneously benign (4). However, colchicine has not been tested for actual post-operative pericardial effusions; therefore, whether the drug reduces their volume and prevents late cardiac tamponade is unknown. A high rate of gastrointestinal adverse effects and drug discontinuations limits the clinical applicability of colchicine in early perioperative care (4). This is why we performed a randomized, double-blinded, placebo-controlled, parallel-group study comparing the efficacy of colchicine and placebo in reducing (POPE) the volume of post-operative pericardial effusion in patients with post-operative effusion persisting >7 days after heart surgery (POPE study).

We performed a first transthoracic echocardiography in 8,140 consecutive patients 7 to 30 days after cardiac surgery. Pericardial effusions were classified into 4 grades, by size and site: grade 1 (minimal), loculated effusion <10 mm; grade 2 (moderate), loculated effusion 10 to 14 mm or circumferential effusion <10 mm; grade 3 (medium sized), loculated effusion 15 to 19 mm or circumferential effusion 10 to 14 mm; and grade 4 (large), loculated effusion ≥20 mm or circumferential effusion ≥15 mm. We included patients only if they showed pericardial effusion of grade 2 or worse (n = 252); 55 were excluded (mainly for consent refusal, indication for immediate pericardial drainage, or colchicine contraindication). Finally, 197 patients (172 were needed by assuming that the spontaneous decrease in mean pericardial effusion grade would be 0.6 grade [5]) were enrolled 16.2 ± 5.3 days after surgery: 98 were randomly assigned to receive colchicine, 1 mg per day, and 99 placebo, for 14 days. The primary endpoint was the difference between treatment groups in mean decrease in pericardial effusion grade from baseline by Mann-Whitney *U* test on an intent-to-treat basis for all 197 patients. Ten patients in the colchicine group and 3 in the placebo group stopped therapy before the end of the study because of new symptoms (mainly digestive) or late withdrawal of consent. However, we obtained baseline and follow-up echocardiograms and clinical follow-up for all.

The 2 groups did not differ in clinical characteristics, type of surgery, or background treatment. The mean age was approximately 64 years, and 86% were male. Surgeries performed were coronary artery bypass graft (n = 110), aortic valve replacement (n = 82), mitral valve surgery (n = 26), and ascending aorta replacement (n = 30); 50 patients had undergone combined surgeries.

Mean pericardial effusion grades at inclusion were 2.9 ± 0.8 and 3.0 ± 0.8 for the placebo and colchicine groups, respectively (p = 0.46), which confirms the large mean pericardial effusion volume at inclusion.

FIGURE 1 Mean Pericardial Effusion Grade Decrease: Comparison Between Colchicine and Placebo Groups



Grade	Placebo	Colchicine	Mean (95% CI)	p
Initial: mean (median)	2.9±0.8 (3[2;4])	3.0±0.8 (3[2;4])		0.46
Final: mean (median)	1.8±1.3 (2[1;2])	1.7±1.2 (1[1;2])		0.47
Change Mean (median)	-1.1±1.3 (-1[-2;0])	-1.3±1.3 (-1[-2;0])	-0.19 (-0.55 to 0.16)	0.23

Values are mean ± SD and (median [25th;75th interquartile range]). Echo = echocardiography.

The main endpoint, mean decrease in pericardial effusion grade from baseline, was −1.1 ± 1.3 and −1.3 ± 1.3, respectively (mean difference between groups −0.19; 95% CI: −0.55 to 0.16; p = 0.23) (**Figure 1**).

In conclusion, among patients with moderate to severe pericardial effusion persisting >7 days after cardiac surgery, colchicine administration did not have a significant effect on evolution of the effusion. (POPE-2 [Colchicine Treatment for Post-Operative Pericardial Effusion]; NCT01266694)

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