Colchicine Acutely Suppresses Local Cardiac Production of Inflammatory Cytokines in Patients with an Acute Coronary Syndrome

Multiple pathways are responsible for inflammation in acute coronary syndromes (ACS). Interleukin (IL) -1β, IL-18, and downstream IL-6 are key inflammatory cytokines in the pathogenesis of coronary artery disease. Colchicine is a simple, inexpensive, yet potent anti-inflammatory drug that is approved for the management of patients with acute gout, and other inflammatory conditions such as pericarditis. Colchicine is believed to block the NLRP3 inflammasome, a cytosolic complex responsible for the production of IL-1β and IL-18. [1, 2]

A study published in Augest 24, 2015 aimed to assess the local cardiac production of inflammatory cytokines in patients with acute coronary syndromes (ACS), stable coronary artery disease and in controls; and determine whether acute administration of colchicine inhibits their production.[3]

In this study; adult patients (>21 years old) with a clinical indication for cardiac catheterization at Royal Prince Alfred Hospital (Sydney, Australia) were invited to participate in the study. According to their clinical presentation they were divided into 3 groups: 40 ACS patients, 33 with stable coronary artery disease, and 10 controls. ACS and stable coronary artery disease patients were randomized to oral colchicine treatment (1 mg followed by 0.5 mg 1 hour later) or no colchicine, 6 to 24 hours prior to cardiac catheterization. Blood samples from the coronary sinus, aortic root (arterial), and lower right atrium (venous) were collected and tested for IL-1β, IL-18, and IL-6 using ELISA. [3]

The results were in ACS patients, coronary sinus levels of IL-1β, IL-18, and IL-6 were significantly higher than arterial and venous levels (P=0.017, <0.001 and <0.001, respectively). Transcoronary (coronary sinus-arterial) gradients for IL-1β, IL-18, and IL-6 were highest in ACS patients and lowest in controls (P=0.077, 0.033, and 0.014, respectively). Also colchicine administration significantly reduced transcoronary gradients of all 3 cytokines in ACS patients by 40% to 88% (P=0.028, 0.032, and 0.032, for IL-1β, IL-18, and IL-6, respectively). [3]

The mechanisms by which colchicine inhibits the production of these cytokines are not completely understood. It has been suggested that

colchicine might block crystal endocytosis and posterior stimulation of the inflammasome complex. Colchicine might have a transcriptional effect by blocking the *MEFV* gene, thereby inhibiting the production of the inflammasome complex proteins. [4,5]

In conclusion; ACS patients exhibit increased local cardiac production of inflammatory cytokines. Short-term colchicine administration rapidly and significantly reduces levels of these cytokines. These data suggest a possible therapeutic role for colchicine in acutely suppressing atherosclerosis-associated inflammation.

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Prepared by Pharm D: Eshraq Alabweeny