Anti-Inflamatory Drug for Myocardial Injury in Acute Coronary Syndrome

*Ryan Ranitya**

Department of Internal Medicine, Bethsaida Hospital, Tangerang, Banten, Indonesia.

***Corresponding Author:**
Ryan Ranitya, MD. Department of Internal Medicine, Bethsaida Hospital. Jl. Boulevard Raya Gading Serpong Kav. 29 Gading Serpong, Tangerang, Banten 15810, Indonesia. Email: rranitya@gmail.com.

Acute coronary syndrome (ACS) as the acute setting of coronary chronic syndrome has been widely known to have high mortality rates. ST-segment elevation of myocardial infarction (STEMI) is one category of ACS that occurs when major coronary arteries are fully blocked acutely and diminish coronary flow leading to myocardial injury and necrosis. Epidemiology data showed that global prevalence varied from 3.8% in patients whose age to 9.5%.[1] The national heart survey of Indonesia also revealed the rising trends of STEMI from 0.63% in 2013 to 1.5% in 2018. STEMI is associated with high mortality despite advanced systems and management such as primary percutaneous coronary intervention (PCI).[2,3]

The high mortality rate of STEMI is frequently due to reperfusion injury, arrhythmia, microvascular obstruction, and myocardial hemorrhage. The myocardial injury is mediated by various pro-inflammatory cytokines or biological agents such as IL-1, TNF-α, and tumor necrosis factors. One of the main key roles in myocardial reperfusion injury is the NLPR3-ASC-caspace inflammation pathway which is a molecular complex that can detect deviation of homeostasis or cellular damage. Numerous studies devoted to investigating the beneficial effect of anti-inflammatory drugs to reducing mortality in STEMI.[4-6]

Colchicine is derived from Colchicum autumnale plant and known for remedies for a long time since 1500 BC. The remedy effect is due to a combination of anti-inflammatory actions. Key actions include decreasing neutrophile L-selectin expression on endothelial cells and interfering with the interaction of neutrophile-platelet which leads to atherothrombosis. The idea to use colchicine in STEMI patients to reduce mortality rate is presumed through this mechanism.[7,8] To date, colchicine is already known to reduce anti-inflammatory markers in ACS. A study by Nidorf et al, investigate the impact of colchicine on High-sensitivity CRP independent of aspirin and atorvastatin in patients with stable coronary artery disease. Drugs targeting inflammation and hs-CRP as anti-inflammation marker indicated suppressing inflammation in the vessel wall.[9,10]

A larger number of patients were involved in a study to investigate plaque stabilization, which is important in acute coronary syndrome. The anti-inflammatory effect of colchicine was presumed to be translating into reducing future coronary events.[11] A nonrandomized observational Study by Vaidya K, et al investigated the effect of colchicine in post-acute coronary syndrome using CT coronary angiography. It showed that colchicine therapy significantly reduced Low attenuation plaque volume (LAPV) Thus, colchicine might be beneficial in secondary prevention.[12]

One of the original articles in this journal is a double-blinded randomized controlled study by Karim B, et al, which investigated the effect of colchicine therapy in reducing reperfusion injury in STEMI who underwent PCI. This well-designed study enrolled 104 patients with STEMI

and after exclusion criteria were applied, the remaining 80 patients were included. They were evenly randomized into two divided arms, the colchicine and the placebo. The colchicine arm patients were given a loading dose of colchicine 2 mg and 0.5 mg/day. The duration of observation was 48 hours to evaluate any reperfusion injury (RI) events such as persistent chest pain, reperfusion arrhythmia, cardiogenic shock, and low-flow thrombolysis. The colchicine failed to show a significant impact in reducing reperfusion injury compared to placebo. This finding was not under other relevant studies. A pilot study, prospective randomized double-blinded, placebo-controlled by Deftereos et al investigated the effect of colchicine in STEMI patients who underwent primary PCI. The results were favorable in terms of reduced myocardial infarct volume size and reduced inflammatory biomarkers.[10] These conflicting results might be caused by several factors including the short duration of observation of the outcome. Percutaneous coronary intervention (PCI) itself as standard therapy had already significant impact in reducing mortality in STEMI patients. [13]

Colchicine is widely known to be safe and effective as an anti-inflammatory drug. Numerous studies have investigated the effect of colchicine in various settings of coronary artery disease. Unfortunately, various results have made it unclear. Meanwhile, the mechanism of colchicine in acute and chronic coronary syndrome needs to be explored comprehensively. The evidence of clinical studies for the beneficial use of colchicine in ACS especially in STEMI is still insufficient. The ongoing studies are worth to have waited for the supporting clinical evidence for the use of colchicine in acute coronary syndrome.

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