

C-Reactive Protein Kinetics: Significance of Light-Dark Variations in C-Reactive Protein in Acute Coronary Syndrome

To the Editor,

We read with great interest the recent article by Sánchez et al¹ on the kinetics of C-reactive protein (CRP) release in the various clinical forms of acute coronary syndrome (ACS). However, we would like to make the following comments.

The article by Sánchez et al¹ discusses CRP kinetics over the entire spectrum of ACS. The authors maintain that CRP concentration at the time of admission was similar in each of the clinical manifestations of ACS, and that the values were influenced by the degree of myocardial necrosis after 12 h from symptoms onset.

The inflammatory substrate of ACS is extremely complex and involves a considerable number of factors related to both activation and modulation. At present, CRP is known to play a role in the pathophysiology of atherosclerosis, as it activates the inflammatory cascade and decreases the synthesis of anti-inflammatory molecules. According to the conditions of the medium in which it acts and the molecular type considered, CRP may have anti-inflammatory or proinflammatory activity (the latter may be humoral or cellular).² Furthermore, it has been shown that CRP concentrations can reach extremely high values in response to various stimuli, with increases up to a thousand-fold.²

The scientific literature has described circadian variations in the circulating concentrations of some cytokines and acute phase reactants.³ However, the existence of circadian variations in circulating CRP concentrations has not been observed in healthy volunteers.⁴ Plasma CRP is produced by hepatocytes, and hepatic synthesis is predominantly under transcriptional control by interleukin-6. In response to appropriate stimuli (eg, myocardial ischemia), around 6 h later this interleukin produces serum CRP concentrations that are increased to above 5 mg/L.⁴

Recent work by our group among patients with ACS has shown daytime variations in serum CRP concentrations.⁵ Serum CRP values were significantly higher in the light phase (9:00 a.m.) when compared to the dark phase (2:00 a.m.), thus indicating that light/dark CRP variations in relation to interleukin-6⁶ are at least partially under neuroen-

doctrines control, in particular, associated with the action of melatonin.⁵

C-reactive protein studies in patients with ACS offer considerable pathophysiologic information on the implication of inflammatory-immunological mechanisms in destabilizing the atherogenic process and the development of vulnerable plaque. Research on the light/dark rhythm of inflammatory-anti-inflammatory molecules in patients with ACS is still in a preliminary stage. These studies unquestionably represent a major stimulus for future research projects and for the eventual development of new therapeutic modalities based on advances made in this important field.

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