

An investigation on interleukin 18 expression in cardiovascular diseases

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Abstract

Introduction: Interleukin 18 is a proinflammatory cytokine from IL-1 cytokine family and plays a central role in inflammation. In fact, it is an IFN-gamma-inducing factor (IGIF). Interleukin 18 increases the response of Th1 cells, cells that are dominant in atherogenesis and cause growth of atherosclerosis plaques. The concentration of circulating IL-18 predicts the probable mortality from cardiovascular problems in CAD patients and plays a key role in atherosclerosis, which is one of the reasons for CHF.

Methods and Results: The proinflammatory cytokines of IL-1 β , TNF- α , IL-6 and LPS induce IL-18 gene expression and IL-18 causes an increase in the proinflammatory cytokines of IL-1 β , IL-6, TNF- α , GM-CSF growth factor, and nitric oxide and cyclooxygenase (cox-2) and thus interleukin 18 causes inflammatory diseases. The Heterodimeric IL-18 receptor is expressed in a variety of cells, including macrophages, T lymphocytes, and NK cells. These cells have a key role in atherosclerotic plaque rupture. The IL-18 binding protein, a natural endogenous inhibitor that is present in high concentration in the extracellular environment and is highly associated with IL-18, interferes with its receptor interaction, thus inhibits IL-18 activity. The level of IL-18 in coronary patients significantly increases and its serum level in CAD patients who die from cardiovascular problems is more than CAD patients who are still alive. In animal models, IL-18 administration has been shown to increase the size and number of clots associated with T lymphocytes and this effect has been eliminated in animals with interferon-gamma deficiency. Angiotensin II increases the expression of IL-18 in arterial smooth muscle cells by AT1 receptors. Losartan will slow down this process. We also know that losartan increases EF and decreases TNF- α and improves left ventricular function in HF patients. It has been shown in a study that stimulation of β -adrenergic receptors by isoproterenol during a series of events increases the transcription and expression of the IL-18 gene, and these events can occur similarly in HF.

Conclusions: There is a strong association between serum IL-18 level and future cardiovascular problems so Inhibition of IL-18 signaling by IL-18 binding protein will be a new therapeutic strategy.

Key words: Interleukin 18, Inflammation, Cardiovascular diseases, Cytokines