Editorial comment

Therapy and clinical trials  Asim K. Duttaroy

Epidemiological and clinical studies have shown strong and consistent relationships between markers of inflammation and risk for cardiovascular disease (CVD) [1]. Recent studies support a central role for inflammation in all phases of the atherosclerotic disease process, from lesion initiation to progression and, ultimately, to plaque rupture and the ensuing thrombotic disorders of CVD [2]. One approach to study of inflammation and CVD is through measurement of circulating inflammatory markers. Several biomarkers linked to inflammation and atherogenesis have been identified. Monocyte chemoattractant protein 1 (MCP-1), produced by endothelial and smooth muscle cells, is a C-C chemokine that mediates monocyte recruitment and entry into vessel walls at sites of atherosclerosis [3]. Although a large number of studies in vitro have focused on the potential role of MCP-1 in pathogenesis, there are no prospective population-based studies investigating the relationship between plasma MCP-1 levels and subclinical atherosclerosis or incidence of coronary heart disease (CHD). Hoogeveen et al. [4] investigated the relationship between MCP-1 level and CHD in a large, prospective, population-based study. In this study, 209 cases with lower-extremity peripheral arterial disease (PAD) and 412 cases with an incidence of CHD were compared with 733 and 709 subjects without PAD and CHD, respectively. Individuals with PAD had significantly higher levels of MCP-1 compared with the group without PAD. They also observed elevated levels of C-reactive protein (CRP) in the plasma of those who also had higher plasma levels of MCP-1. However, more clinical studies are required to assess whether intervention targeting MCP-1 is beneficial in the treatment of atherosclerosis.

CRP is an acute-phase protein that is produced in response to acute injury, infection or other inflammatory stimuli. CRP has been shown in prospective cohort and case-control studies to be a reliable measure of underlying systemic inflammation and a strong predictor of future cardiovascular events [5–7]. These observations stimulated interest in a possible role for CRP in CVD risk assessment in clinical practice [5–7]. Although most studies have shown that CRP is a strong and independent predictor of atherosclerotic risk, the recent study by Wilson et al. [8] showed that the elevated CRP level did not provide any further prognostic information beyond traditional risk-factor assessment to predict future major CHD in a prospective, observational cohort study. They used a total of 1949 men and 2497 women without CVD from the Framingham study who underwent CVD risk-factor assessment.

Obesity contributes to the occurrence of atherosclerotic and hypertensive disease and it is now considered to be a serious health problem, especially in the industrialized world. Panagiotakos et al. [9] observed an association between inflammation and obesity status in a population-based sample of 3042 adults without CVD. They observed several inflammatory markers to correlate with central adiposity, irrespective of age, sex, or various metabolic or lifestyle variables.

Hall et al. [10] examined whether administration of isoflavones reduces endothelial inflammation in post-menopausal women. In contrast to previous findings, these workers did not find any beneficial effects of supplementation of isoflavones on plasma levels of intercellular cell-adhesion molecule 1 (ICAM-1), vascular cell adhesion molecule 1 (VCAM-1), E-selectin, or MCP-1. However, plasma CRP levels were reduced in these women after isoflavone supplementation. They observed that the effects of isoflavone supplementation depend on the genotype of the woman. Analysis of key selected genotypes in this population of postmenopausal women indicated a significant diet–gene interaction for isoflavones between the ERβ AluI genotypes. Isoflavones reduced plasma VCAM-1 in the variant AA genotype but not in the homozygous wild-type (GG) or heterozygous (GA) genotypes. It seems that certain subpopulations may respond more beneficially to isoflavone supplementation by decreasing plasma VCAM-1 levels in one genotype of the ERβ AluI polymorphism.
2  Bimonthly update

References

Recommended reading

Hall WL, Vafeiadou K, Hallund J, et al. Soy-isoflavone-enriched foods and markers of lipid and glucose metabolism in postmenopausal women: interactions with genotype and equol production. Am J Clin Nutr 2006; 83:592–600. This study did not find any beneficial effects of supplementing isoflavones on circulating concentrations of ICAM-1, VCAM-1, E-selectin, or MCP-1 in postmenopausal women. Analysis of key selected genotypes in this population of postmenopausal women indicated a significant diet–gene interaction for isoflavones between the ERβ AluI genotypes with isoflavones reducing plasma VCAM-1 in the variant AA genotype but not the homozygous wild-type or heterozygous genotypes.

Hoogeveen RC, Morrison A, Boerwinkle E, et al. Plasma MCP-1 level and risk for peripheral arterial disease and incident coronary heart disease: Atherosclerosis Risk in Communities study. Atherosclerosis 2005; 183:301–307. This paper provides data supporting the general hypothesis that increased expression of MCP-1 is part of an inflammatory system which plays a critical role in the etiology of atherosclerosis through increased recruitment of mononuclear leucocytes to sites of vascular injury. In this study, 209 cases with lower-extremity PAD and 412 cases with incident of CHD were compared with 733 and 709 subjects without PAD and CHD, respectively. Individuals with PAD had significantly higher levels of MCP-1 compared with the group without PAD.

Libby P. Inflammation and cardiovascular disease mechanisms. Am J Clin Nutr 2006; 83:456S–460S. This paper suggests that inflammation is central to the progression from fatty streak to complex plaque. The author suggests that assessment and management of CVD risk must evolve in step with a greater understanding of pathophysiologic mechanisms. Inflammatory markers such as CRP merit careful consideration for inclusion in our risk-assessment algorithms. Roles of inflammation in the initiation and development of atherosclerosis are now increasingly recognized in treating CVD patients.


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