EFFECT OF ATORVASTATIN ON C-REACTIVE PROTEIN IN CORONARY HEART DISEASE PATIENTS

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Summary

C-reactive protein (CRP) is a unique risk marker in inflammation and coronary heart disease and plays a vital role in the pathogenesis of cardiovascular disease. CRP has a wide variety of biological properties and functions. Inflammation is one of the keystones in the etiology and pathogenesis of atherosclerosis, which led to worldwide attention being focused on CRP and its role in the process of atherosclerosis. CRP plays a role in the expression of different adhesion molecules on endothelial cells and the protein is able to activate human complement within the plaque. It has been proven that an elevated CRP level, with a cut-off point of approximately 2.6 mg/L, is associated with cardiovascular disease.

Key Words: Atorvastatin, C-reactive protein, Coronary heart disease, Low-density lipoprotein

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Introduction

Atorvastatin, a well-known statin, commonly used to lower plasma low-density lipoprotein (LDL) cholesterol levels by inhibition of HMG-CoA reductase. Atorvastatin is also used to reduce the risk of coronary heart disease (CHD). [1] Prevalence of CHD is 9.0% in the urban and 3.3% in the rural population. [2] It is estimated to be the most common cause of death globally by 2020. Atorvastatin is highly soluble and permeable, and completely absorbed after oral administration but extensive first-pass metabolism in the gut wall as well as in the liver, as oral bioavailability is only 14%. Atorvastatin has an apparent volume of distribution 6.5 L/kg, total plasma clearance 625 mL/min, plasma protein binding 98%, and the half-life ($t_{1/2}$) approximately 7 hours after oral administration. Atorvastatin is metabolized by cytochrome P450 (CYP) 3A4. [1, 3]

C-reactive protein (CRP) is a unique risk marker in inflammation and CHD and plays a vital role in the pathogenesis of cardiovascular disease. [4] The predictive value of plasma CRP as a risk factor for cardiovascular events has led some researchers to support the use of CRP as a main cardiovascular risk assessment tool, along with total cholesterol HDL ratios and homocysteine levels. [5] Atorvastatin treatment decreases CRP level in addition to decreasing low-density lipoprotein (LDL) cholesterol may further decrease CHD risk. CRP belongs to a family of cyclic pentameric proteins known as pentraxins, and is considered to play a significant role in innate host defense and in the pathogenesis of inflammation and atherosclerosis. The normal value of CRP concentrations in plasma is ≤2 mg/L, increasing in the value of CRP from >2.6 mg/L increased the chance of CHD events. [4, 6]

Mechanism of action of Atorvastatin

Atorvastatin inhibit 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the rate limiting enzyme in cholesterol synthesis (reduces the production of mevalonic acid from HMG-CoA); this then results in a compensatory increase in the expression of LDL receptors on hepatocyte membrane and increase LDL catabolism. [1-7]

Effects of Atorvastatin on CRP level

The predictive value of plasma CRP is a risk factor for cardiovascular events, along with serum total cholesterol, LDL- cholesterol, VLDL-cholesterol, HDL-cholesterol, lipoprotein (a) and homocysteine levels. Serum concentrations of CRP reflect in part vascular inflammation. Statins reduce CRP levels by up to 60%. CRP reduction is independent of LDL-C lowering, and variation between statins in CRP reduction may play some role in CVD event reduction rates. [4-6]
High dose atorvastatin significantly decreased CRP (≤2 mg/L) during the early days of acute coronary syndromes than the low dose atorvastatin and therefore improve CHD risk reduction in high-risk patients. A study showed, that atorvastatin significantly reduce the incidence of postoperative arterial fibrillation (AF) and postoperative peak CRP level. [7-8]
The degree of CRP reduction obtained depends on the particular statin and dose used in study. A study compared the effects of various statins on CRP levels in patients with CHD. Atorvastatin 40 mg/day produced significantly greater CRP reductions than 40 mg/day of fluvastatin, lovastatin, pravastatin, or simvastatin; this reduction was independent of LDL-C changes. [9]
A clinical study conducted on statins derivatives simvastatin (20 mg/day), pravastatin (40 mg/day), and atorvastatin (10 mg/day), on levels of high-sensitive CRP showed that with each drug CRP levels were significantly decreased after treatment with all 3 statins compared with baseline (figure 1). [10]

Conclusion

CRP is an independent unique risk marker of various cardiovascular events. Decreases CRP with statin therapy is associated with decreased risk of CHD events in patients. Atorvastatin treatment reduces CRP secretions in adipocytes, possibly through lowering blood cholesterol (VLDL-cholesterol) levels. Atorvastatin produces greater reductions in CRP at lower dose than other statins. From these finding we can conclude that atorvastatin shows higher efficacy than other statin derivatives in CHD patients.

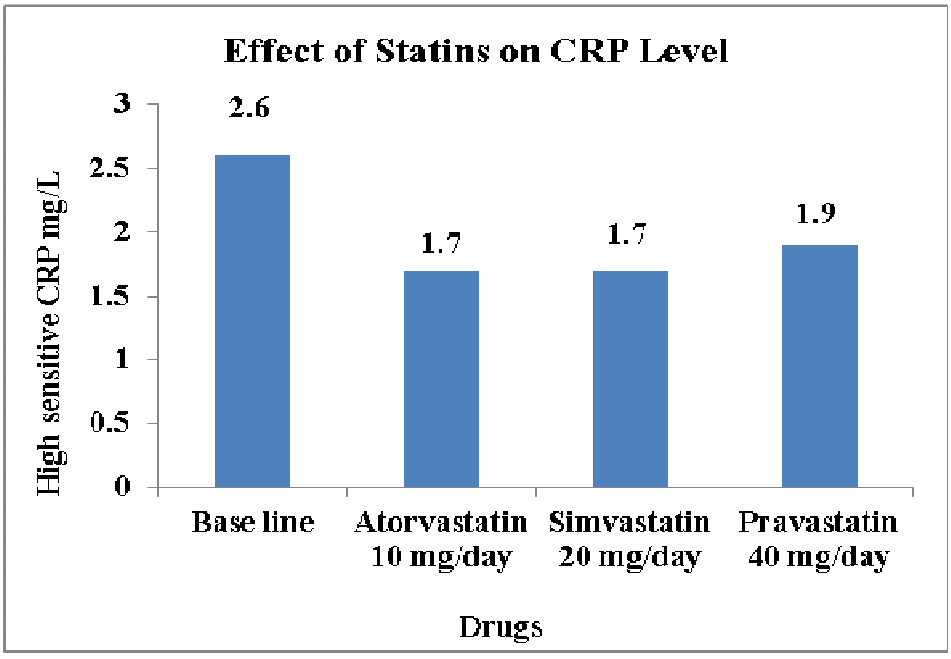

Figure 1: Effect of statins derivatives on C-reactive protein levels

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