Effect of atorvastatin on hs-CRP in acute coronary syndrome

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Markers of inflammation are being investigated as predictors of coronary ischaemic events. All major statins have shown almost similar and significant efficacy in reducing C-reactive protein (CRP) concentrations in acute coronary syndrome (ACS), but atorvastatin was used in a high dose (80 mg).
- This study was designed to evaluate the effect of a lower dose (20 mg) of atorvastatin on hs-CRP concentrations in patients with ACS.

WHAT THIS STUDY ADDS

- A lower dose of atorvastatin (20 mg) was effective in decreasing hs-CRP and LDL concentrations in as short a duration as 4 weeks. The use of a lower dose of atorvastatin in patients of ACS can offer an attractive approach for early treatment of ACS patients.

AIMS

To evaluate the effect of a lower dose (20 mg) of atorvastatin on hs-CRP concentrations in patients with ACS.

METHODS

Group A ($n = 50$) patients received atorvastatin 20 mg day⁻¹ for 4 weeks in addition to standard anti-anginal treatment. Group B ($n = 50$) patients received standard anti-anginal treatment without atorvastatin.

RESULTS

hs-CRP concentrations decreased in both groups, but the decrease was greater in group A. The decrease in hs-CRP was also significantly greater in the subgroups of smoking, hypertension and past history of cardiovascular disease with atorvastatin.

CONCLUSIONS

The use of a lower dose (20 mg) of atorvastatin can offer an attractive approach for early treatment of patients with ACS.

Introduction

C-reactive protein (CRP) has emerged as a very important marker of inflammation. Concentrations of highly sensitive (hs)-CRP correlate strongly with increased vascular event rates in patients with acute coronary syndrome (ACS) [1].

Anti-inflammatory effects of statins characterized by CRP lowering have generated maximum interest in reducing coronary events [1, 2]. All major statins have shown

almost similar efficacy in reducing CRP concentrations, using equipotent doses [3]. However, atorvastatin in a high dose (80 mg) is the most widely investigated drug for reducing hs-CRP in ACS. It was largely believed that high doses of statins were needed to exert their pleiotropic effects, but high dose of statins have additional risk of increased adverse effects and more drug interactions [4]. Hence this study was designed to evaluate the effect of lower dose (20 mg day⁻¹) of atorvastatin on hs-CRP in patients with ACS.

Methods

This prospective, open study was conducted on 100 patients enrolled over a period of 15 months. The study protocol was approved by the institutional ethics committee. Patients diagnosed with ACS as per WHO criteria were included [5]. Patients were enrolled after they signed an informed written consent.

In group A ($n = 50$), patients with $LDL > 100 \text{ mg dl}^{-1}$ were administered atorvastatin 20 mg day^{-1} for 4 weeks in addition to standard anti-anginal treatment. In group B ($n = 50$), patients with $LDL \leq 100 \text{ mg dl}^{-1}$ were given standard anti-anginal treatment but not atorvastatin. Dietary advice was given to all patients.

After enrolment the hs-CRP and lipid profile were analyzed at 0 and 4 weeks. The incidence of recurrent myocardial infarction (MI), recurrent angina, stroke, mortality and treatment emergent adverse effects was recorded as secondary variables.

Data analysis

Data were analyzed using Student's *t*-test and analysis of variance (ANOVA) and chi-square test. Correlation coefficients (*r*) were calculated for alterations in hs-CRP and LDL concentrations.

Results

The groups were comparable at baseline (Table 1). At the end of treatment, the mean hs-CRP in group A decreased by 82% ($P < 0.001$) from 2.32 ± 0.26 to $0.57 \pm 0.16 \text{ mg dl}^{-1}$. In group B, the mean hs-CRP decreased by 54% ($P < 0.001$) from 1.91 ± 0.20 to $1.04 \pm 0.15 \text{ mg dl}^{-1}$. At end of the study hs-CRP concentrations were significantly lower in group A as compared with group B.

Table 1

Baseline characteristics of patients in group A (atorvastatin) and group B (without atorvastatin)

Characteristics	Group A (atorvastatin) ($n = 50$)	Group B (without atorvastatin) ($n = 50$)
Age (years) (mean $\pm$ SEM)	56.0 ± 1.52	57.5 ± 1.6
>40 years	46 (92%)	47 (94%)
Sex (M : F)	34 : 16	38 : 12
STEMI	24 (48%)	20 (40%)
Diagnosis		
NSTEMI	1 (2%)	1 (2%)
Unstable angina	25 (50%)	29 (58%)
Risk factors		
Diabetes mellitus	17 (34%)	11 (22%)
Hypertension	22 (44%)	20 (40%)
Smoking	15 (30%)	17 (34%)
Family history of CAD	15 (30%)	14 (28%)
Past history of CVD	13 (26%)	16 (32%)

* $P < 0.05$ as compared with group A. CAD, coronary artery disease; CVD, cardiovascular disease; NSTEMI, Non ST elevation myocardial infarction; STEMI, ST elevation myocardial infarction.

In a subgroup analysis (Figure 1), the mean percentage decrease in hs-CRP in smokers, hypertensives and patients with a past history of cardiovascular disease (CVD) after 4 weeks of treatment with atorvastatin was significantly greater as compared with group B. There was significant decrease in total cholesterol (25%) and LDL in group A (38%) and increase in LDL (29%) in group B. There was no significant correlation between the change in CRP and LDL in either of the groups. There were no cases of recurrent MI, stroke or mortality in either group. There was no significant difference between the two groups regarding incidence of adverse effects.

Discussion

In the present study decrease in hs-CRP was significantly greater with atorvastatin as compared with the group given no atorvastatin. The greater reduction of hs-CRP in group A is likely to be caused by additional pleiotropic effects of atorvastatin. Other studies have reported a mean decrease of 22–40% in hs-CRP with different doses of atorvastatin given for 4 weeks [2, 6].

The difference between degree of fall in hs-CRP in our study and other studies could be attributed to the fact that we included only ACS patients and different statins can have variable anti-inflammatory effects at variable doses. The decrease in hs-CRP concentration in group B could be because of anti-inflammatory properties of drugs or due to stabilization of plaque [7, 8].

In a poststudy subgroup analysis, atorvastatin significantly decreased hs-CRP concentrations in patients with a history of smoking, hypertension and past history of CVD. As reported earlier, there was a significant decrease in LDL and total cholesterol with atorvastatin in our study [2–4].

Figure 1

Mean percentage decrease in plasma hs-CRP in the subgroups. Group A Atorvastatin, (▨); Group B Without atorvastatin, (▤)

Our study showed no significant difference between the secondary outcome measures between the two groups, but the short duration of study may not be appropriate to comment on this.

Correlation analysis of various investigators has strongly suggested that the statin mediated reduction in CRP is unlikely to be a secondary consequence of a reduction in LDL, but rather is potentially mediated by independent pathways [9]. In subanalyses of the PROVE IT trial, it was demonstrated that patients who achieved lower CRP concentrations regardless of achieved LDL had better clinical outcomes than those with elevated CRP. There is evidence of incremental benefit for those in whom statin therapy resulted in CRP concentrations of less than 0.2 mg dl^{-1} , whether or not LDL cholesterol concentrations were also reduced to the target value of less than 70 mg dl^{-1} [10]. In our study, patients assigned to receive 20 mg atorvastatin daily were more likely to achieve these values.

To conclude, the use of a lower dose atorvastatin in patients with ACS can offer an attractive approach for early treatment, but needs more exploration. The ongoing 15 000 patient rosuvastatin in the primary prevention of cardiovascular disease among patients with low concentrations of LDL and elevated hs-CRP (JUPITER) trial will hopefully add a wealth of data to help understand better the roles and interplay of inflammation, C-reactive protein, statins and coronary artery disease [9].

Competing interests: none to declare.

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