The benefits of statin treatment on cardiac function in chronic heart failure: a meta-analysis of randomized controlled trials

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Abstract

Purpose Whether additional benefit can be achieved with the use of statin in patients with chronic heart failure (CHF) remains undetermined. The purpose of this meta-analysis is to evaluate the beneficial role of statin on cardiac function in CHF patients.

Methods Pubmed, MEDLINE, EMBASE, and EBM Reviews databases were searched for randomized controlled trials comparing statin treatment with non-statin treatment in patients with CHF. Additional studies from cited references were also identified. Two reviews independently assessed studies for inclusion and performed data extraction. Weighted mean differences (WMD) with 95% confidence intervals (CI) were calculated using random effects models.

Results Eleven trials with 590 patients were included. Pooled analysis showed that statin therapy was associated with significant increase in left ventricular ejection fraction (LVEF) (WMD = 3.35%, 95% CI 0.80% to 5.91%, P = 0.01). The beneficial effects of statin treatment were also demonstrated by the reduction of left ventricular end-diastolic diameter (LVEDD) (WMD = -1.00 mm, 95% CI -2.34 to 0.34 mm, P = 0.18), left ventricular end-systolic diameter (LVESD) (WMD = -2.57 mm, 95% CI -8.02 to 3.09 mm, P = 0.18), B type natriuretic peptide (BNP), and NYHA functional class. At end points were based on the change from baseline to follow-up, and pooled effects were presented as weighted mean differences (WMD) with 95% confidence intervals (CI) using random effect models. Meta-regression and sensitivity analyses (including exclusion of 1 study at a time) were conducted to explore heterogeneity. Finally, on the basis of the data on LVEF, publication bias was tested using the Beggs adjusted rank correlation test and Egger regression asymmetry test. P values were 2-tailed, the statistical significance was set at 0.05. All analyses were performed with STATA software 9.0.

Methods

We performed a literature search in Pubmed, MEDLINE, EMBASE, and EBM Reviews databases to July 2009. Search terms were “statin”, “heart”, “cardiac”, “dysfunction”, “insufficiency”, “inadequacy”, and “failure” without restrictions of language and publication form. The reference lists of studies that met our inclusion criteria were also searched for potentially relevant trials.

Studies were included in our analysis if they met the following criteria: (1) the design was a prospective, randomized controlled trial; (2) patients with established CHF, no matter what the etiology, were assigned to statin treatment or control (non-statin treatment or placebo) in addition to concurrent therapy; and (3) they reported data on left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), B type natriuretic peptide (BNP), or NYHA functional class.

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Results

The overall pooled results with random-effects analysis showed that additional statin therapy was significantly superior to standard medical therapy in terms of LVEF improvement, with a clinically and statistically significant difference of 3.35% (95% CI 0.80 to 5.91%, P = 0.01, I2 = 98.9%) (Figure 2). Furthermore, statin therapy was similarly found to have benefits concerning LVESD (WMD = -3.77 mm, 95% CI -6.24 to -1.31 mm, P = 0.003, I2 = 99.5%) (Figure 3). LVESD (WMD = -3.77 mm, 95% CI -6.37 to -0.76 mm, P = 0.01, I2 = 97.2%) (Figure 4), BNP were (WMD = -2.08 pg/ml, 95% CI -4.12 to -0.04 pg/ml, P = 0.0001, I2 = 96.3%), as compared with control.

Introduction

Despite advances in therapy, chronic heart failure (CHF) remains a major cause of morbidity and mortality in the worldwide, CHF is associated with activation of oxidative stress, proinflammatory cytokines, and neurohormones. In view of this, hydroxymethylglutaryl coenzyme A reductase inhibitors (statins) are considered as a promising candidate for the treatment of CHF, on account of that statins exert diverse cellular cholesterol-independent effects throughout the cardiovascular system encompassing enhancement of nitric oxide (NO) synthesis, improvement of endothelial function, inhibition of inflammatory cytokines, and restoration of impaired autonomic function.

Previous experimental studies have revealed that statin may attenuate pathologic myocardial remodeling and promote cardiac function in heart failure. Thereafter, numerous trials have been conducted to determine the beneficial role of statin on the failing myocardium in CHF patients, however, the results were conflicting. In order to provide a more robust estimate of the potential benefits of statin therapy, we performed a meta-analysis of randomized controlled trials to evaluate the impact of statin treatment on cardiac function-related parameters in patients with CHF.

Results

The flow of selection of studies for inclusion in the meta-analysis is shown in Figure 1. Of the initial 4205 hits, 11 randomized controlled trials (RCTs) with a total of 590 patients satisfying the inclusion criteria were identified and analyzed. No significant differences were seen between the groups assigned statins and placebo in background CHF therapies, including angiotensin converting enzyme inhibitor (or angiotensin receptor blocker) and Beta-blocker therapy. Moreover, there were only 3 studies that utilized rosuvastatin, cerivastatin, and simvastatin separately, while the rest of included trials focused on atorvastatin. Additionally, most of the patients enrolled in this meta-analysis had normal levels of low-density lipoprotein (LDL).

Methods

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Studies were included in our analysis if they met the following criteria: (1) the design was a prospective, randomized controlled trial; (2) patients with established CHF, no matter what the etiology, were assigned to statin treatment or control (non-statin treatment or placebo) in addition to concurrent therapy; and (3) they reported data on left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), B type natriuretic peptide (BNP), or NYHA functional class.

All end points were based on the change from baseline to follow-up, and pooled effects were presented as weighted mean differences (WMD) with 95% confidence intervals (CI) using random effect models. Meta-regression and sensitivity analyses (including exclusion of 1 study at a time) were conducted to explore heterogeneity. Finally, on the basis of the data on LVEF, publication bias was tested using the Beggs adjusted rank correlation test and Egger regression asymmetry test. P values were 2-tailed, the statistical significance was set at 0.05. All analyses were performed with STATA software 9.0.

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Conclusion

Statin therapy confers benefits not only in increasing LVEF, but also in reducing LVESD, LVEFSD, BNP and NYHA functional class in CHF patients. Furthermore, the improvement of LVEF associated with statin treatment might be time-dependent. These results suggest that statin therapy may be a potential novel treatment strategy for CHF patients.