REVIEW

The Effect of Statins on Erectile Dysfunction: A Meta-Analysis of Randomized Trials

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ABSTRACT

Introduction. Erectile dysfunction (ED) is common in older men, especially those with comorbidities such as diabetes and atherosclerotic disease, conditions where statins are frequently prescribed.
Aim. To examine the effect of statin therapy on ED using the five-item version of the International Inventory of Erectile Function (IIEF).
Methods. We performed a random-effects meta-analysis of studies identified by a systematic search of MEDLINE, Web of Knowledge, the Cochrane Database, and ClinicalTrials.gov. Examination of the 186 retrieved citations resulted in the selection of 11 randomized trials for inclusion in the meta-analysis.
Main Outcome Measures. Change in the IIEF score.
Results. IIEF increased by 3.4 points (95% CI 1.7–5.0, $P = 0.0001$) with statins compared to control. This effect remained statistically significant after multiple sensitivity analyses, including analysis for publication bias, a cumulative meta-analysis, and 11 repeated analyses with each study omitted sequentially. The increase in IIEF with statins was approximately one-third to one-half of that previously reported with phosphodiesterase-5 inhibitors and larger than the effect of lifestyle modification. Metaregression showed an increase in benefit with decreasing lipophilicity. The average age of participants and the degree of LDL cholesterol lowering did not alter the effect on IIEF.
Conclusion. Statins cause a clinically relevant improvement of erectile function as measured by the five-item version of the IIEF. **Kostis JB and Dobrzynski JM. The effect of statins on erectile dysfunction: A meta-analysis of randomized trials. J Sex Med 2014;11:1626–1635.**

Key Words. Statins; Erectile Dysfunction; Meta-Analysis; International Index of Erectile Function

Introduction

Erectile dysfunction (ED) is prevalent among older men, especially those with metabolic syndrome, diabetes, or cardiovascular disease, and it is expected to become more frequent worldwide [1–4]. Erectile dysfunction not due to psychogenic causes or to prostatectomy is usually due to endothelial dysfunction [5,6]. Atherosclerotic disease and ED have similar risk factors, including diabetes, smoking, obesity, hypertension, and endothelial dysfunction, as well as hypercholesterolemia [7,8]. Many patients with ED are prescribed statins, as ED is common among patients with coronary artery disease, cerebrovascular disease, and peripheral vascular disease [9,10]. Statins improve endothelial function through lowering of low density lipoprotein (LDL) levels and possibly through pleiotropic effects related to increased availability of nitric oxide [11–13]. Statins decrease morbid and mortal cardiovascular events [14]. The above considerations imply that statins would have a positive effect on patients with ED. However, there are reports of higher rates of ED among statin users [15,16]. In addition, the lipophilicities of individual statins may affect their metabolic effects [17,18].

As some studies report impaired erectile function among statin users while others report a beneficial effect, we performed a meta-analysis of the

effects of statins on ED as ascertained by the five-item version of the International Index of Erectile Function (IIEF), a widely used multidimensional self-report instrument [19].

Methods

Studies Included in the IIEF Meta-Analysis and Data Extraction

Using the PRISMA guidelines, a systematic search of MEDLINE, Web of Knowledge, the Cochrane Database, and ClinicalTrials.gov was performed for the intersects of the term "erectile dysfunction" with the term "statin" and with the names of each of the marketed statins individually (atorvastatin, cerivastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin) through the end of March 2013 (Figure 1, Supporting Information Table S1). We excluded studies in animals, basic science or nutrition studies, reviews, editorials, case reports, and studies without ED as an outcome. Of the 116 records that were screened, 43 were excluded on reading the title or the abstracts. The remaining 73 full-text articles were evaluated by both authors. The data were entered independently by each author in a specifically constructed database, with disagreements adjudicated during face-to-face meetings. Eligible studies were not excluded for size or performance bias. In one study, data were included for only 113 of 173 participants. Complete follow-up was available in all other randomized trials. Sixty-one of the 73 were excluded for the following reasons: in 36, ED, as it pertained to statin use, was not an outcome; 25 were reviews, editorials or letters; 14 were carried out in animals or pertained to basic research or nutrition; and two presented the data of studies already included in the analysis. Sixteen studies were excluded for more than one of the above reasons. Eleven studies were used in the meta-analysis [20–28], including two reports that tested separate interventions [26,28]. Of the 11 randomized trials, seven were double-blind placebo-controlled [20–22,24,26,27], and four used no medication [23,25,28] as the control. The three observational studies were not included in the primary analysis [18,29,30]. A secondary analysis including the three observational studies in addition to the randomized trials was also performed.

Statistical Methods

Statistical analyses were done using JMP version 9 and Comprehensive Meta-Analysis version 2.2 (BioStat, Englewood, NJ, USA). The primary outcome examined was change in IIEF score. Cumulative meta-analysis was performed, with the studies ordered according to decreasing width of the confidence interval. To investigate whether one study biased the results, we performed the

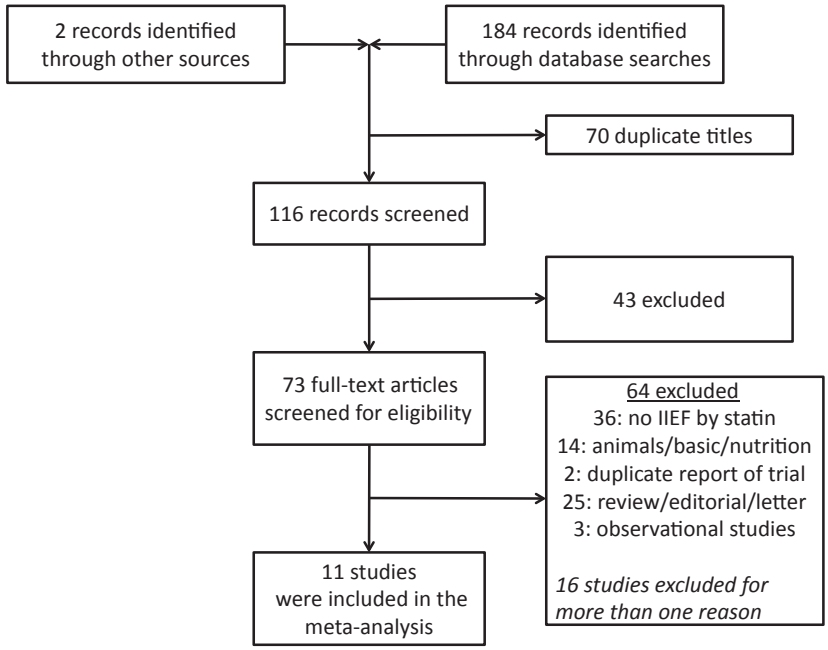

Figure 1 Flowchart of study selection.