REVIEWS

The Effect of Statins on Erectile Dysfunction: A Systematic Review and Meta-Analysis

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ABSTRACT

Introduction. It is not known if statins will improve symptoms in patients with established erectile dysfunction (ED).
Aim. We carried out a systematic review and meta-analysis to assess the effect of statins on ED.
Methods. A literature review was performed to identify all published randomized double-blind, placebo-controlled trials of statins for the treatment of ED. The search included the following databases: MEDLINE, Embase, and the Cochrane Controlled Trials Register. The reference lists of the retrieved studies were also investigated. A systematic review and meta-analysis were conducted.
Main Outcome Measures. Six publications involving a total of 462 patients were used in the analysis, including three randomized controlled trials (RCTs) that compared statins with placebo and three RCTs that compared statins plus sildenafil with placebo plus sildenafil.
Results. For the comparison of statins (+/− sildenafil) with placebo (+/− sildenafil), the mean International Index of Erectile Function (IIEF-5) (the standardized mean difference [SMD] = 3.23, 95% confidence interval [CI] = −1.65 to 4.80, $P < 0.0001$) indicated that statins (+/− sildenafil) showed statistically significantly greater improvements in the mean IIEF-5 compared with placebo (+/− sildenafil). For the comparison of statins with placebo, the mean IIEF-5 (SMD = 2.13, 95% CI = −1.46 to 5.73, $P = 0.24$) indicated that there was no significant difference in erectile function between the statins and placebo. For the comparison of statins plus sildenafil with placebo plus sildenafil, the mean IIEF-5 (SMD = 3.60, 95% CI = 2.64 to 4.56, $P < 0.00001$), the IIEF domain (SMD = 4.88, 95%CI = 3.01 to 6.74, $P < 0.00001$), and the global efficacy question (odds ratio = 6.44, 95% CI = 2.92 to 14.23, $P < 0.00001$) showed that compared with placebo plus sildenafil, statins plus sildenafil clearly improved erectile function.
Conclusions. This meta-analysis indicates that statins (+/− sildenafil) may improve ED compared with placebo (+/− sildenafil). **Cui Y, Zong H, Yan H, and Zhang Y. The effect of statins on erectile dysfunction: A systematic review and meta-analysis. J Sex Med 2014;11:1367–1375.**

Key Words. Statins; Erectile Dysfunction; Hypercholesterolemia; Meta-Analysis; Randomized Controlled Trial

Introduction

Erectile dysfunction (ED) is defined as the persistent inability to achieve or maintain an erection for satisfactory sexual performance [1]. ED affects 30 million men in the United States and 150 million worldwide. This number is expected to increase as the population ages [2]. The common underlying cause is thought to be related to vascular abnormalities of the penile blood supply and erectile tissue [3]. American Urology Association updated guidelines recommend phosphodiesterase type 5 (PDE5) inhibitors as first-line therapy for ED. These agents are orally active and self-administered on an as-needed basis prior to sexual intercourse [4,5].

Statins use results in reduction of hepatic synthesis of cholesterol, with a compensatory increase on the membrane of hepatocytes in the number of receptors with a high affinity for low-density lipoprotein (LDL). Currently, the number of molecules available has a similar chemical structure,

although differing in pharmacokinetics and drug interactions [6].

Epidemiological studies have shown that elevated serum cholesterol and reduced high-density lipoprotein cholesterol levels are associated with an increased risk of ED [7,8]. Whether correcting a dyslipidemic profile will result in a reduced risk of developing ED has not been established. Similarly, it is not known if such an intervention will improve symptoms in patients with established ED. The situation is further complicated by the likelihood that one of the rarer side effects of statins is ED [9].

Gupta et al. [10] conducted a meta-analysis and proved that lifestyle modification and pharmacotherapy for cardiovascular (CV) risk factors are effective in improving sexual function in men with ED [11,12]. To our knowledge, this is the first work that has systematically assessed through meta-analysis the effect of statins on ED, which may resolve some of the current controversies over use of the drug.

Materials and Methods

Search Strategy

MEDLINE (1966 to July 2013), Embase (1974 to July 2013), and Cochrane Controlled Trials Register databases were searched by two of the authors to identify randomized controlled trials (RCTs) that referred to the impact of statins in treating ED; we also searched the reference lists of the retrieved studies. The following search terms were used: *statins*, *erectile dysfunction*, *randomized controlled trial*.

Inclusion Criteria and Trial Selection

RCTs that met the following criteria were included: (i) the study design included treatment with statins; (ii) the study provided accurate data that could be analyzed, including the total number of subjects and the values of each index like the International Index of Erectile Function (IIEF-5), IIEF domain and global efficacy question (GEQ) (yes); and (iii) the full text of the study could be accessed. When the same study was published in various journals or in different years, the most recent publication was used for the meta-analysis. If the same group of researchers studied a group of subjects with multiple experiments, then each study was included. As the data we need were all included in the trials, we did not contact authors for additional information. Also, trial registries were searched if the included articles did not provide them. Decisions on trials to include were taken unblindly by the authors. Disagreements were resolved by discussion. A flow diagram of the study selection process is presented in Figure 1.

Quality Assessment

The quality of the retrieved RCTs was assessed using the Jadad scale [13]. All the identified RCTs were included in the meta-analysis regardless of the quality score. The methodological quality of each study was assessed according to how patients were allocated to the arms of the study, the concealment of allocation procedures, blinding, and data loss due to attrition. The studies were then classified qualitatively according to the guidelines published in the *Cochrane Handbook for Systematic Reviews of Interventions* v.5.1.0 [14]. Based on the quality assessment criteria, each study was rated and assigned to one of the three following quality categories: A, if all quality criteria were adequately met, the study was deemed to have a low risk of bias; B, if one or more of the quality criteria was only partially met or was unclear, the study was deemed to have a moderate risk of bias; or C, if one or more of the criteria was not met or not included, the study was deemed to have a high risk of bias. Differences were resolved by discussion among the authors.

Data Extraction

The following information was collected for each study by a different person: (i) the name of the RCT; (ii) the study design and sample size; (iii) the therapy that the patients received; (iv) the country in which the study was conducted; and (v) data including the IIEF-5, IIEF domain, and GEQ (yes). Appropriate methodology according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement [15] was adhered to. The outcome of interest was ED score based on the IIEF-5, IIEF domain, and GEQ (yes).

Statistical Analysis and Meta-Analysis

The meta-analysis of comparable data was carried out using RevMan v.5.1.0 (Cochrane Collaboration, Oxford, UK) [14]. Changes in the IIEF-5, IIEF domain, and GEQ were determined as differences between baseline (study entry) and study completion. We estimated the relative risk for dichotomous outcomes and the standardized mean difference (SMD) for continuous outcomes pooled across studies using the DerSimonian and Laird