The Association of Statin Use and Gonado-Sexual Function in Women: A Retrospective Cohort Analysis

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ABSTRACT

Introduction. It has been hypothesized that statins reduce sex hormone biosynthesis through hepatic inhibition of cholesterol synthesis, which is a precursor of androstenedione and estradiol. Such a reduction has been associated with menstrual irregularities, menopausal disorders, infertility, and low libido, but studies are conflicting. Few studies have evaluated the clinical effects of statins on gonadal-sexual function in women.

Aim. To compare the risk of gonado-sexual dysfunction in statin users vs. nonusers.

Methods. This was a retrospective cohort study of all female, adult patients (30–85 years) enrolled in the Tricare Prime/Plus San Antonio catchment area. Using 79 baseline characteristics, we created a propensity score-matched cohort of statin users and nonusers. The study duration was divided into a baseline period (October 1, 2003 to September 30, 2005) to describe patient baseline characteristics and a follow-up period (October 1, 2005 to March 1, 2012) to determine patient outcomes. Statin users were defined as those prescribed a statin for ≥3 months between October 1, 2004 and September 30, 2005. Logistic regression was used to determine the association of statin use with patient outcomes.

Main Outcome Measures. Outcomes included menstrual disorders, menopausal disorders, infertility, and ovarian/sexual dysfunction during the follow-up period. Outcomes were identified using inpatient or outpatient *International Classification of Diseases*, *Ninth Revision*, *Clinical Modification* codes as defined by the Agency for Healthcare Research and Quality's Clinical Classifications Software.

Results. Of 22,706 women who met study criteria, we propensity score-matched 2,890 statin users with 2,890 nonusers; mean age 58 ± 12 years. Statin use was not significantly associated with menstrual disorders (OR 0.97; 95% CI 0.81–1.16), menopausal disorders (OR 0.92; 95% CI 0.83–1.02), infertility (OR 0.79; 95% CI 0.36–1.73), or ovarian/sexual dysfunction (OR 1.18; 95% CI 0.83–1.70).

Conclusions. Statin use was not associated with higher risk of gonado-sexual dysfunction in women. **Ali SK, Reveles KR, Davis R, Mortensen EM, Frei CR, and Mansi I. The association of statin use and gonado-sexual function in women: A retrospective cohort analysis. J Sex Med 2015;12:83–92.**

Key Words. Menstrual Disorders; Menopausal Disorders; Infertility; Ovarian Dysfunction; Sexual Dysfunction; Statin

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Introduction

Sexual and gonadal health is important to overall physical and emotional well-being in women. Approximately 40 million women in the United States are affected by sexual dysfunction [1]. Furthermore, disorders associated with hormone depletion and imbalances are common. It is estimated that 70–90% of women in their childbearing years in the United States experience menstrual irregularities or other menstrual disorders [2]. In addition, approximately 75% of peri- and post-menopausal women experience symptoms associated with menstrual cycle cessation and hormone depletion, namely vasomotor symptoms [3]. Finally, sexual and gonadal dysfunction can significantly affect quality of life [4,5].

Sex hormones play a key role in female sexual and reproductive health. Depletion or irregularities in female sex hormone production have been implicated in a host of disorders, including menstrual and menopausal disorders, infertility, ovarian insufficiency, and sexual dysfunction [1,6,7]. Specifically, reductions in estrogens or androgens in females have been associated with menstrual irregularities, menopausal disorders, infertility, and low libido [8–13]. It has been hypothesized that HMG-CoA reductase inhibitors (i.e., statins) affect sex hormone biosynthesis, primarily due to hepatic inhibition of cholesterol synthesis, which is a precursor of androstenedione and estradiol [14]. Prior studies have demonstrated that low-density lipoprotein (LDL) is used preferentially as a precursor for ovarian steroid biosynthesis [15]. Therefore, the reduction of LDL by statins may result in an overall reduction of female sex hormones, including androgens and estrogens, but studies are conflicting. In contrast, statins increase nitric oxide production in endothelial cells [16], which may aid in improving sexual dysfunction and vasomotor symptoms in females; however, clinical data to support this hypothesis are lacking. However, the relation between hormonal levels and sexual dysfunction is not necessarily a direct one. For example, a recent meta-analysis noted that statins may improve sexual dysfunction in men [17], despite a reduction in testosterone levels [18].

The objective of this study was to examine the risks of gonado-sexual dysfunction among female statin users and nonusers in a large cohort of patients from a single-payer health system.

Methods

Study Design

The study was approved by the Brooke Army Medical Center Institutional Review Board, San Antonio, Texas and the VA North Texas Health Care System, Dallas, Texas. This was a longitudinal, retrospective cohort study of patients enrolled in the San Antonio Tricare Prime/Plus catchment area from October 1, 2003 to March 1, 2012. The data source we used for this study was the Military Health System Management Analysis and Reporting Tool (M2). This system is an ad hoc query tool comprised of outpatient medical records, inpatient medical records, benefits claims for health care delivered outside the military health system, laboratory data, and pharmacy data. The laboratory data include all tests performed within the military health-care system and results of those tests. Pharmacy data include all pertinent patient demographics and medication dosing information regardless of point-of-care location. The M2 application has been previously used for administrative monitoring, outcome tracking, and correlational research [19–22]. A full description of database characteristics has been published previously [23].

The study was divided into two time periods. First, baseline patient characteristics were collected between October 1, 2003 and September 30, 2005. A second follow-up period from October 1, 2005 to March 1, 2012 was used to assess patient outcomes.

Patient Population

Female patients were included in this study if they (i) were enrolled in Tricare Prime/Plus from beginning of fiscal year (FY) 2003 until FY 2010 in the San Antonio catchment area; (ii) were 30 to 85 years old; (iii) had at least one outpatient visit during both the baseline and follow-up periods; and (iv) received at least one prescription medication during the baseline period. Since all included patients existed in the system regardless of point of care location or affiliation, there were no missing data and no imputation was utilized. Since all included patients were actively enrolled as Tricare Prime/Plus beneficiaries from FY2003–FY2010, patients who died during the study period would have not been included.

Three groups of patients were excluded from the study. First, we excluded trauma and burn patients, as patient outcomes may be attributed to the severity of the trauma or burn rather than