ORIGINAL RESEARCH—MEN'S SEXUAL HEALTH

Persistent Sexual Side Effects of Finasteride: Could They Be Permanent?

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ABSTRACT

Introduction. Finasteride has been associated with sexual side effects that may persist despite discontinuation of the medication. In a clinical series, 20% of subjects with male pattern hair loss reported persistent sexual dysfunction for ≥6 years, suggesting the possibility that the dysfunction may be permanent. These subjects also reported a wide range of symptoms including changes in cognition, ejaculate quality, and genital sensation. Other medications have been associated with irreversible neurological effects, such as phenothiazines with tardive dyskinesias.

Aim. To prospectively study whether the persistent sexual side effects associated with finasteride resolve or endure over time.

Methods. Subjects (N = 54) with persistent sexual side effects associated with finasteride were reassessed after 9–16 months (mean 14 months). All subjects were otherwise healthy young men without any baseline sexual dysfunction, medical conditions, psychiatric conditions, or use of oral prescription medications prior to taking finasteride for male pattern hair loss.

Main Outcome Measure. Scores from the Arizona Sexual Experience Scale (ASEX).

Results. The participation rate was 81%. At reassessment persistent sexual side effects continued to be present in 96% of subjects. According to the ASEX scores, 89% of subjects met the definition of sexual dysfunction. Neither the length of finasteride use nor the duration of the sexual side effects correlated to changes in scores of sexual dysfunction.

Conclusion. In most men who developed persistent sexual side effects (≥3 months) despite the discontinuation of finasteride, the sexual dysfunction continued for many months or years. Although several rat studies have shown detrimental changes to erectile function caused by 5 alpha reductase inhibitors, the persistent nature of these changes is an area of active research. Prescribers of finasteride and men contemplating its use should be made aware of the potential adverse medication effects. **Irwig MS. Persistent sexual side effects of finasteride: Could they be permanent? J Sex Med 2012;9:2927–2932.**

Key Words. Finasteride; Sexual Dysfunction; Neurosteroids; Low Libido; Erectile Dysfunction

Introduction

Finasteride is a 5 alpha reductase inhibitor used in the treatment of male pattern hair loss (MPHL) and benign prostatic hypertrophy. Finasteride blocks the conversion of testosterone to the more potent androgen dihydrotestosterone (DHT) in many tissues including the skin, hair follicles, and prostate. Lesser known effects of the 5 α reductase inhibitors are that they also block the conversion of progestogens and glucocorticoids: progesterone to 5α-dihydroprogesterone and deoxycorticosterone to 5α-dihydrodeoxycorticosterone, respectively.

When Propecia was approved for the treatment of MPHL, it was known through several double-blind randomized controlled trials that it may cause a small but significant amount of sexual dysfunction with libido, orgasm, and erectile problems [1–3]. These trials reported that the sexual

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side effects resolved with time or with discontinuation of finasteride. Since Propecia's release, postmarketing surveillance has found that a subset of young men who take finasteride experience persistent sexual side effects despite the discontinuation of the medication [4,5]. Unfortunately, less common adverse effects of a medication are often only uncovered after several thousands of patients have been exposed to the medication [6]. In April of 2011 the product labeling for Propecia in the United States was updated to include the side effect of "difficulty in achieving an erection that continued after stopping the medication."

While the incidence of persistent sexual side effects associated with finasteride is unknown, it is very likely that over 1,000 men worldwide are experiencing the effects. This estimate is based upon the number of registered users (N = 2,170) on the Internet forum Propeciahelp.com which focuses on "persistent sexual, mental and physical side effects which continue despite quitting" finasteride [7]. Although it is difficult to ascertain how many of the registered users on the Propeciahelp.com forum suffer from the medication effects, 1,000 is likely a gross underestimate as many sufferers have not stumbled upon the Web site, do not surf English Web sites due to language barriers, or are skeptical to register sensitive personal information on an online forum.

Irreversible neurological effects of a medication have been reported and studied with tardive dyskinesias, which are caused by the use of phenothiazines for treatment of schizophrenia [8]. In a gerbil model, a 30-day course of finasteride caused persistent changes in the structural and ultrastructural morphology of the prostate [9]. There is a solid and growing body of basic science evidence that finasteride reduces the concentrations of several neuroactive steroids that play a role in neurogenesis and neuronal survival. Male mice treated with finasteride had reversibly lower levels of brain DHT and less neurogenesis as demonstrated by fewer young neurons in the hippocampus [10]. Likewise, finasteride lowers the concentration of 3α5α tetrahydroprogesterone, otherwise known as allopregnanolone (ALLO), a downstream metabolite of dihydroprogesterone that protects neurons from apoptosis via the Bcl-2 and Bcl-xL genes [11].

Aims

This study was designed to prospectively follow men with persistent sexual side effects of finasteride to see whether their sexual dysfunction would resolve, improve, or remain diminished over time.

Methods

Subjects

Participants for this study reported sexual side effects associated with finasteride which persisted for at least 3 months despite cessation of the medication. The indication for the medication was MPHL, and all men started and completed finasteride use before age 40. Men were excluded from the study if they reported any of the following before starting finasteride: baseline sexual dysfunction, chronic medical conditions, psychiatric conditions, a history of taking psychiatric medications or baseline use of non-topical prescription medications other than a short course of antibiotics.

Subjects were recruited from a previous study (N = 54) relating to persistent sexual side effects of finasteride [4]. Most subjects were initially recruited from Propeciahelp.com, an Internet forum dedicated to unresolved side effects of finasteride. Other subjects were recruited from the author's clinical practice and from physician referrals. All subjects provided written consent to this study which was approved by the university's institutional review board.

Design

Telephone or spoken Skype standardized interviews were conducted with all subjects as previously described [4]. Subjects were asked about demographic information, medical and psychiatric histories, medication use, and sexual function before and after finasteride. Follow-up e-mails were sent to participants 9–16 months (mean 14 months) after their initial interview dates to reassess their sexual function. Subjects were asked to readminister the Arizona Sexual Experience Scale (ASEX). The ASEX consists of five questions that measure core elements of sexual function: libido, arousal, erectile function, ability to reach orgasm, and orgasm satisfaction [12]. Each domain was measured bimodally, with a six-point Likert scale ranging from hyperfunction (1) to hypofunction (6). Sexual dysfunction was present if the total score was ≥19 or if any one item was ≥5 or if any three items were ≥4. The sensitivity and specificity of this instrument to identify sexual dysfunction were 82% and 90%, respectively [12]. The validation of ASEX consisted of a control group of 16 men with a mean age of 38 [12]. Their mean scores