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Emotional Consequences of Finasteride: Fool's Gold

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Abstract

Androgenetic alopecia, the gradual, progressive loss of hair frequently results in psychological despair, in part related to changes in self-image. Current androgenetic alopecia treatments are limited to hair transplantation and medications that inhibit dihydrotestosterone, a potent androgen associated with follicular micronization. Users of finasteride, which prevents dihydrotestosterone production, report serious physical and emotional adverse effects, collectively known as post-finasteride syndrome. Psychiatric illnesses and personality traits, specifically neuroticism influence emotional well-being. Limited research exists exploring the psychological corollaries of post-finasteride syndrome and preexisting Axis I and Axis II mental health conditions. The aim of this study was to explore how having a preexisting personal and/or familial history of a psychiatric diagnosis and certain personality traits may influence anxiety and depression among finasteride users. Participants in this online survey completed the Beck Depression Inventory, the Beck Anxiety Inventory, and Ten-Item Personality Inventory. An important finding in this study was that almost 57% (n = 97) of men reported a psychiatric diagnosis and 28% (n = 27) had a first-degree relative with a mental health disorder, of this group 17 only had a family history. Nearly 50% of the men surveyed reported clinically significant depression as evidenced by Beck Depression Inventory score and 34% experienced anxiety on the Beck Anxiety Inventory. There were no statistically significant trends in personality traits reported. Results provide evidence on the need to screen for psychiatric history and counseling patients about the potential psychological consequences of finasteride. Prescribing clinicians should carefully weigh the risk/benefit ratio with these patients.

Keywords

finasteride, androgenetic alopecia, post-finasteride syndrome

Introduction

Androgenetic alopecia (AGA), also known as male pattern hair loss, is a common dermatologic complaint that affects approximately 30% of the male population by the age of 30 years; the prevalence increases to about 50% by the age of 50 years (Ellis, Sinclair, & Harrap, 2002). In men suffering from AGA, the course of hair loss is often unpredictable, with periods of remission and exacerbations, and in about 20% of cases, hair loss becomes permanent (Picardi, Abeni, Melchi, Puddu, & Pasquini, 2000).

Both men and women often regard healthy hair as an important attribute of their own and others' appearance and physical attractiveness. Healthy hair contributes significantly to an individual's sense of identity, self-esteem, and body image; psychologically, "a full head of hair" often represents strength, youth, and virility (Mannes, 2013). The loss of hair has few harmful physical effects; however, several studies report that men who experience the premature loss of hair express significant concern and emotional distress (Karaman, Dereboy, Dereboy, & Carman, 2006; Kranz, 2011). Men who experience AGA report difficulties with social and familial relationships as well as frequent bantering from peers about their condition (Cash, 1992; van der Donk, Passchier, Dutree-Meulenberg, Stolz, & Verhage, 1991).

Studies investigating AGA have reported that individuals frequently make judgments about another's personality and capabilities based on their hair. In one study, men with AGA were rated less favorably on physical attributes, attractiveness, likeability, and potential for life success (Cash, 1990). Studies investigating the psychosocial effects of AGA among men report higher scores on measures of anxiety and depression and poor body image (Cash, 1999; Hunt & McHale, 2005). A number of studies have reported that there is an increased tendency toward hypochondriasis and interpersonal conflicts, stress, and

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depression (Budd, Himmelberger, Rhodes, Cash, & Girman, 2000; Cash, 1999). There is evidence that those with AGA experience suicidal ideation more frequently and are at greater risk of suicide (Muscarella & Cunningham, 1996).

Among several factors that contribute to AGA, genetic heritability is the most common (Banka, Bunagan, & Shapiro, 2013). Hair loss in those who have inherited the trait is gradual and progressive, beginning with increased hair shedding followed by a transition from the growth of thick, pigmented hair to the progression of thinner, shorter hairs and, eventually, nonpigmented vellus hair and, in some complete denudation (Banka et al., 2013). There are few treatments that successfully improve AGA. Despite our limited understanding of AGA's etiology, researchers investigating the underlying causes of AGA point to an overabundance of the testosterone derivative dihydrotestosterone (DHT) in the follicle of hair as the principle cause. An excess of DHT is believed to contribute to follicular miniaturization resulting in the prevention of new hair growth and maturation. DHT conversion occurs with the assistance of the enzyme Type II 5-α *reductase*.

In 1997, the U.S. Food and Drug Administration approved finasteride 1 mg per day for the treatment of AGA, a medication that has been marketed under the brand name Propecia. Finasteride, a Type II 5-α *reductase* inhibitor, blocks the enzyme responsible for converting testosterone into the more potent androgen DHT and has been used successfully in the treatment of hair loss. Since U.S. Food and Drug Administration approval, finasteride has been associated with several common side effects, including a decrease in libido, trouble achieving or maintaining an erection or both, and a decrease in the amount of seminal volume; all of these symptoms may occur while taking the medication and persist after cessation. The only nervous system/psychiatric adverse effect listed on the product warning label is "depression."

Several research studies have investigated the adverse psychological effects of finasteride (Altomare & Capella, 2002; Ganzer, Jacobs, & Iqbal, 2014; Irwig, 2012; Melcangi et al., 2013; Rahimi-Ardabili, Pourandarjani, Habibollahi, & Mualeki, 2006; Traish, Hassani, Guay, Zitzmann, & Hansen, 2011). In 2002, researchers investigating depression as an adverse effect of finasteride, researchers reported that men (n = 17) who had taken 1 mg per day of finasteride for AGA developed moderate to severe depression during treatment and stated that further studies were needed (Altomare & Capella, 2002). In 2012, Irwig compared rates of depressive symptoms and suicidal thoughts in two groups, men who had taken finasteride and those who had not. Using the Beck Depression Inventory–II (BDI-II), Irwig (2012) reported that rates of depressive symptoms (BDI-II score ≥ 14) were significantly higher among former finasteride users (75%; 46/61) as compared with the control group (10%; 3/29; $p < .001$). The author concluded that patients taking this medication may experience depressive symptoms and suicidal thoughts, and clinicians should advise patients of potential of the risk of adverse side effects.

Research has established associations between personality traits, primarily neuroticism, and mental health (Pavot, Diener, & Fujita, 1990; Steel, Schmidt, & Shultz, 2008). There are three hypothesized causal links between neuroticism and adverse outcomes related to mental health. A genetic polymorphism for neuroticism may predispose an individual to comorbid mental health conditions, specifically anxiety and depression (Hettema, Neale, Myers, Prescott, & Kendler, 2006). Persons suffering with high neuroticism have also been associated with experiencing more pronounced and less well-regulated responses to stressful life events (Khan, Jacobson, Gardner, Prescott, & Kendler, 2005; Zautra, Affleck, Tennen, Reich, & Davis, 2005). Individuals with high neuroticism have been reported to experience clinical traits similar to the psychiatric condition, generalized anxiety disorder (Hettema, Prescott, & Kendler, 2004; Lahey, 2009).

Several studies examining personality traits and hair loss describe the impact of AGA as psychologically distressing. Symptoms include being overwhelmed by depression, feelings of anxiety, social phobia, adjustment and paranoid disorders, having more neurotic tendencies, and experiences of conflict with their societal environment, more often than the general population (Alfani et al., 2012; Picardi et al., 2000; Ruiz-Doblado, Carrizosa, & Garcia-Hernandez, 2003). The objectives of the present study were (a) to determine whether men who have taken finasteride for AGA report high levels of anxiety and depression and (b) to examine correlates among preexisting mental health diagnoses (depression and anxiety), and the personality trait, neuroticism.

Method

Design/Participants

This is the second part of an initial web-based survey conducted to describe the global physical and psychological effects of finasteride, also known as post-finasteride syndrome (PFS). The study received approval from the institutional review board of the City University New York, Hunter College. Study participants were recruited in two ways. Initially, an e-mail with a link to the study was sent to 150 patients who had sought medical care at the office of one of the authors for persistent adverse effects related to the use of finasteride taken to treat AGA. The survey link was posted on Propeciahelp.com, an

online forum for exchange of information about unresolved side effects of finasteride. Participants included in the study were male, 18 years and older, had a history of taking finasteride 1 mg for AGA for at least 3 months, and had reportedly experienced persistent adverse effects. Exclusion criteria included a history of baseline sexual dysfunction and/or nonconfirmed psychiatric diagnosis. Once the link was accessed, a written consent form was provided informing the participant that completion of the questionnaire implied informed consent to participate in the study. As a reminder, the survey was sent out again after 6 weeks to minimize nonresponse bias. To describe study population, demographic characteristics (age, education, race and ethnicity, sexual orientation, and general health) were collected and medically confirmed psychiatric diagnosis of participant and any first-degree relatives (Ganzer et al., 2014).

In this study, psychological sequelae were assessed using two self-report scales, the BDI and the Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988). The BDI, a 21-item multiple choice self-report questionnaire tests for depressive symptomology; hopelessness, irritability, thoughts such as guilt, as well as physical symptoms fatigue, loss of weight, and low libido (Beck, 1972). Scoring is divided into six categories: normal (0-10), mild mood disturbance (11-16), borderline clinical depression (17-20), moderate depression (21-30), severe depression (31-40), and a score >40 representing extreme depression. The measure has been reported to have good internal consistency with a mean coefficient of $\alpha = .86$ for psychiatric patients and .81 for nonpsychiatric participants (Beck, Steer, & Carbin, 1988).

The BAI, selected to evaluate anxiety, is a 21-item self-report questionnaire that distinguishes anxious diagnostic groups (e.g., panic disorder) from nonanxious diagnostic groups (e.g., major depressive disorder). The inventory is broken down into three categories: very low anxiety (0-21), moderate anxiety (22-35), and sums exceeding 35 having a potential cause for concern. Its instrument has good internal consistency with a $\alpha = .92$, and test–retest reliability of $r = .75$ (Beck, Epstein, et al., 1988).

Participants' personality traits, specifically neuroticism, were explored using the Ten-Item Personality Inventory (TIPI) to assess the personality domains: openness, conscientiousness, extraversion, agreeableness, and neuroticism also known as the "Big Five" (Gosling, Rentfrow, & Swann, 2003). The TIPI uses a 7-point Likert-type scale ranging from 1 (*disagree strongly*) to 7 (*agree strongly*). For each of the five dimensions, participants respond to each item by using the common stem "I see myself as . . . " with each item having two descriptors (e.g., for Extroversion, "extroverted, enthusiastic") for each of the five dimensions with two-item subscales for each category (e.g., Neuroticism and Emotional stability). The scale has been extensively used in research, has good construct validity and the test–retest correlations for the TIPI were significant, with the mean $r = .72$ (Gosling et al., 2003). For all five subscales, higher scores reflect stronger personality traits. Data were analyzed using the Statistical Package for Social Science (SPSS) software version 16.00 (SPSS Inc., Chicago, Illinois). All surveys were reviewed for completeness prior to inclusion in analysis and listwise deletion used to remove any cases with missing values. Descriptive statistics were used to summarize the demographic characteristics of the study sample.

Results

This study expands on the previously reported results (Ganzer et al., 2014). A subset of men in the initial study ($n = 97$) completed a second online survey that specifically sought to explore the psychological and emotional effects of finasteride. All study participants were male, had reportedly taken the medication finasteride, 1 mg for AGA for at least 3 months, and sought treatment for both physical and psychological symptoms after having stopped the medication. In this study, overall men reported that they were generally in good health, 89.7% ($n = 87$) with 86.2% ($n = 68$) holding a high school degree or higher. To determine history of psychiatric complaints, participants were asked whether they had a medically confirmed psychiatric diagnosis. This was asked to determine whether or not a preexisting condition and/or if a first-degree relative that also suffered with a medically confirmed psychiatric diagnosis since an aim of this study was to establish whether a preexisting condition or familial history may contribute to increased anxiety and depression after taking finasteride. Both Axis I diagnoses (e.g., Major Depressive Disorder) and Axis II personality disorders were targeted. Fifty-five percent ($n = 53$) of participants confirmed that they had an established psychiatric diagnosis prior to initiating therapy with finasteride with 28.8% ($n = 27$) confirming a psychiatric diagnosis in a first-degree relative. An interesting finding in the second group was that 63% ($n = 17$) of these men reported only having a family history, 11 of which had both personal and family history of a medically confirmed psychiatric diagnosis. Evaluation of mood disturbance following treatment and discontinuation of finasteride revealed that overall 49.3% ($n = 48$) reported a BDI score of clinical significance (BDI ≥ 21), with a mean of 16.8 ($SD = 15.86$). Of particular concern was that clinically, 38 were in the moderate to severe range and 5 participants scored greater than 40, placing them within the extreme depression range. Participants reported BAI scores of 16.5% ($n = 16$) moderate anxiety and

17.5% (n = 17) potential cause for concern. In addition, there was a significant correlation between the BDI and BAI (r = .75, p < .0001).

Contrary to the study hypothesis that participants would score high on neuroticism, TIPI scores reflected that participants were extroverted, mean of 3.5, SD = 1.35; agreeable, mean of 4.1, SD = 1.16; were emotionally stable, mean of 4.8, SD = 1.27; and open to experiences, mean of 3.9, SD = 1.39.

In addition to the measures, an open-ended question asked participants to share information qualitatively about the experience of having taken finasteride. Ninety-six percent (n = 93) of respondents posted anecdotal comments after completing the survey. Responses were categorized to determine "themes" and subthemes. The thematic process of repetition was carried out to look for "recurring regularities" or exemplars in the text (Lincoln & Guba, 1985). Analysis revealed that respondents expressed an overall "despair," "fear" with the subtheme of "hopelessness." Examples of statements of despair were "It's the single worst thing that has and will ever happen to me," "It's practically killed me, cost me every bit of money I had and ruined my emotional relationship for life," "I'm very scared I won't be able to make it through this," and "This disease has ripped my life away." These accounts further support the experience of a depressed affect among this cohort and the importance of understanding the mental health consequences of this medication.

Discussion

This study set out to describe symptoms of depression and anxiety among a sample of men who had taken finasteride for AGA and stopped taking the medication after experiencing negative symptoms. Results of this study further support previous reports that finasteride is associated with changes in affect, including depression and anxiety (Ganzer et al., 2014; Irwig, 2012; Rahimi-Ardabili et al., 2006; Römer & Gass, 2010). In an attempt to further characterize these men, information about personal and familial history of a medically diagnosed psychiatric condition was collected. To the authors' knowledge, this is the first study that explored preexisting familial mental health conditions and psychological health among users of finasteride. Of particular interest is that in this study, more than half of the participants reported having a preexisting medically confirmed psychiatric diagnosis and that almost 30% indicated that they had a first-degree relative with an established psychiatric history. The existence of premorbid mental health conditions among users of finasteride may expose a subset of men who possess a selective independent brain-based vulnerability to finasteride that puts them at increased risk of developing clinically significant emotional changes post-finasteride. Further complicating the matter is that PFS has been associated with either low or borderline testosterone levels among men who have stopped the medication resulting in hypogonadotropic hypogonadism. These low levels of gonadal hormones have themselves been attributed to cause men to experience depression, anxiety, and a decrease in quality of life (Aydogan et al., 2012). These important factors may constitute a *perfect storm* leading to the development of an anomalous emotional response in these men after stopping finasteride. Additionally, the Big Five personality traits were explored using the TIPI. Participants in this study scored within previously reported normed ranges for all five-factor TIPI scores. The observation that neuroticism was not at all overly prevalent in these PFS sufferers further implicates Axis I psychopathology, as opposed to Axis II, as the marker that may confer an anomalous brain substrate that renders such men intrinsically more vulnerable to emotional disorders arising from finasteride exposure. The TIPI is a brief self-report test and future research should employ measures that can provide a more in-depth tool to explore relationships between the construct of personality traits, specifically neuroticism and severity of behavioral symptoms.

There are several noted limitations in the present study. This study used a cross-sectional design and the use of a comparison group would allow for a more causal analysis of results. One such group that interests us is the much larger, and considerably older, population of men who use finasteride in higher dosage, 5 mg/d, to effectively treat benign prostatic hypertrophy. Since benign prostatic hypertrophy generally affects men as they age and is a common condition, we would expect to find a considerably lower prevalence of Axis I personal and/or family history in this group. To our knowledge, there are no studies analyzing PFS in this group of men. The current sample size is relatively small (n = 97) and therefore not nationally representative of a factor that influences generalizability. Additionally, the study's web-based self-report design may have missed some individuals that failed to fully disclose psychological symptoms. Future research should take these factors into consideration.

Conclusion

It has been reported that markers of anomalous brain substrate, such as left handedness, skeletal asymmetry, or a family history of major mood disorders, are greatly overrepresented in the histories of women with severe, debilitation premenstrual tension syndromes compared with women without premenstrual dysphoric disorder (Hay, Bancroft, & Johnstone, 1994; Klein, Versi, & Herzog, 1999; Robinson & Ismail, 2015). Similarly, this

exploratory study suggests an analogous association, by which possession of a familial and/or a personal history of an Axis I mental health disorder, becomes an independent marker of anomalous brain substrate that, by some as of yet unknown mechanism, puts them at increased risk of experiencing intractable emotional disorders triggered by finasteride therapy.

Future research is clearly needed to further elaborate these risk factors that confer adverse, persistent behavioral outcomes on the men who use finasteride to fight baldness and to understand the mechanisms that underlie this association. One hypothesis is that epigenetic factors may contribute to these symptoms. However, in the meantime and given the current results, prescribing clinicians are well advised to obtain past and familial psychiatric histories from patients pursuing finasteride therapy and factor this marker of anomalous brain substrate in to the discussion of potential long-lasting, adverse effects from finasteride, prior to prescribing it for AGA.

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