
To whom it may concern,

I am suffering from persistent health problems after taking and stopping Finasteride. Thousands of patients across the world have reported similar symptoms and this is currently termed "Post-Finasteride Syndrome" (PFS). The symptoms range in severity between patients and include serious physical, sexual and cognitive health problems.

Why this happens to certain people is still being investigated. There is no known effective and safe treatment.

Attached to this letter are abstracts from case control studies and two literature reviews that provide the current scientific understanding of the condition.

More information on the subject can be found at www.pfsnetwork.org.

I would please ask that my adverse drug reaction is recorded and reported to the appropriate pharmacovigilance agencies.

Thank you very much for your understanding and support,

Yours sincerely

Differential Gene Expression in Post-Finasteride Syndrome Patients (Howell et al. 2021)

Source: <https://pubmed.ncbi.nlm.nih.gov/34247957>

Abstract

Background:

An organic etiology underpinning post-finasteride syndrome, a constellation of persistent sexual, neuropsychiatric, and somatic symptoms reported by men exposed to 5-alpha-reductase inhibitors (5ARIs), is debated. Persistent changes in neurosteroid levels or androgen receptor expression have been implicated.

Aim:

To determine whether differences in gene expression, especially in relevant biologic pathways, exist between patients reporting post-finasteride syndrome symptoms and healthy controls.

Methods:

This was a single center, prospective case-control study taking place between March 2013 and September 2018. Men 18 years and older being evaluated for sexual dysfunction (study) or circumcision (control) were eligible for inclusion. Twenty-six men with a history of 5ARI use reporting symptoms consistent with post-finasteride syndrome were included in the patient group. Twenty-six men consented to inclusion in the control group.

Outcomes:

The primary outcome measure is gene expression data for genes affecting neurosteroid levels and androgen receptor activity from penile skin cells.

Results:

Gene expression of cells from penile skin samples from twenty-six men of median age 38 years (IQR, 33-42) in the study group was compared with that from twenty-six men of median age 41 years (IQR, 35-62) in the control group ($P = .13$), with 1,446 genes significantly over-expressed and 2,318 genes significantly under-expressed in study patients. Androgen receptor expression was significantly higher in study patients compared to controls (9.961 vs 9.494, adjusted P value = .01). Serum levels of androgen receptor activity markers 5α -

androstenediol (0.950 ng/mL [0.749-1.587] vs 0.949 [0.817-1.337], $P = .34$) or 3α -androstenedione (3.1 ng/mL [1.925-5.475] vs 6.7 [3.375-11.4], $P = .31$) revealed no significant differences. No significant differences were found between the number of trinucleotide repeats (21.5 [20-23.75], 22 [19-25], $P = .94$).

Clinical implications:

In this study we present evidence of gene expression correlating with observed biologic differences in patients with post-finasteride syndrome; providers who prescribe 5ARIs should be aware and advise their patients accordingly.

Strengths & limitations:

Strengths of this study include the evaluation of multiple proposed etiologies for post-finasteride syndrome. The study is also strengthened by the fact that not all data matched the initial hypotheses, qualifying the argument for the existence of PFS. Limitations include potential selection bias arising from more severe phenotypes seeking care; lack of gene expression data prior to 5ARI exposure; lack of non-penile tissue samples supposedly involved; and a lack of mechanistic data to imply causality.

Conclusion:

This study is the first to consider and demonstrate gene expression differences in patients with PFS as a potential etiology of sexual dysfunction.

Post-finasteride Syndrome: A Review of Current Literature (Than et al. 2018)

Source: <https://link.springer.com/article/10.1007/s11930-018-0163-4>

Abstract

A constellation of persistent adverse effects—collectively termed post-finasteride syndrome (PFS)—after 5 α -reductase inhibitor treatment for benign prostatic hyperplasia (BPH) and androgenic alopecia (AGA) has recently been described. The severity of these sexual, physical, neurological, and psychiatric side effects raises important concerns regarding the treatment of these conditions, especially given the prevalence of indications for these medications. Here we review the literature exploring the symptoms, proposed mechanisms, and potential disease modulating factors for PFS.

While the persistent sexual side effects associated with PFS are well documented, research on the physical, neurological, and psychiatric adverse effects is much less ubiquitous. Though the mechanisms leading to PFS have been proposed, a clear treatment plan for these patients has not been established. In the treatment of BPH and AGA with 5 α -reductase inhibitors, the risks of PFS should be considered.

The occurrence of persistent adverse sexual, physical, neurological, and psychiatric side effects after 5 α -reductase inhibitor is well supported by the existing data. While additional studies are needed to better evaluate the role of 5 α -reductase inhibitors in the manifestation of the symptoms of PFS, the risks of PFS should be critically evaluated when treating patients with BPH or AGA.

Neuroactive steroid levels and psychiatric and andrological features in post-finasteride patients (Melcangi et al. 2017).

Source: <https://www.sciencedirect.com/science/article/abs/pii/S0960076017301024>

Abstract

Recent reports show that, in patients treated with finasteride for male pattern hair loss, persistent side effects including sexual side effects, depression, anxiety and cognitive complaints may occur. We here explored the psychiatric and andrological features of patients affected by post-finasteride syndrome (PFS) and verified whether the cerebrospinal fluid (CSF) and plasma levels of neuroactive steroids (i.e., important regulators of nervous function) are modified. We found that eight out of sixteen PFS male patients considered suffered from a DSM-IV major depressive disorder (MDD). In addition, all PFS patients showed erectile dysfunction (ED); in particular, ten patients showed a severe and six a mild-moderate ED. We also reported abnormal somatosensory evoked potentials of the pudendal nerve in PFS patients with severe ED, the first objective evidence of a neuropathy involving peripheral neurogenic control of erection. Testicular volume by ultrasonography was normal in PFS patients. Data obtained on neuroactive steroid levels also indicate interesting features. Indeed, decreased levels of pregnenolone, progesterone and its metabolite (i.e., dihydroprogesterone), dihydrotestosterone and 17beta-estradiol and increased levels of dehydroepiandrosterone, testosterone and 5alpha-androstane-3alpha,17beta-diol were observed in CSF of PFS patients. Neuroactive steroid levels were also altered in plasma of PFS patients, however these changes did not reflect exactly what occurs in CSF. Finally, finasteride did not only affect, as expected, the levels of 5alpha-reduced metabolites of progesterone and testosterone, but also the further metabolites and precursors suggesting that this drug has broad consequence on neuroactive steroid levels of PFS patients.

The Post-finasteride Syndrome: Clinical Manifestation of Drug-Induced Epigenetics Due to Endocrine Disruption (Traish, 2018)

Source: <https://link.springer.com/article/10.1007/s11930-018-0161-6>

Abstract

Post-finasteride syndrome (PFS) is a disorder characterized by a set of clinical symptoms experienced during use or after drug discontinuation. This cluster of symptoms encompasses overall sexual dysfunction (SD), erectile dysfunction (ED), loss of libido, depression, suicidal ideation, anxiety, panic attacks, insomnia, and cognitive dysfunction. To date, there is lack of comprehensive understanding of the biochemical and pathophysiological mechanisms responsible for the adverse effects of finasteride. More importantly, there is lack of knowledge and effective clinical tools for treatments of this condition, resulting in outright dismissal of complaints by individuals afflicted with this syndrome. Psychological symptoms and cognitive dysfunction of PFS are far more serious and difficult to treat than sexual dysfunction symptoms and may lead young men to contemplate, attempt, or even commit suicide. Therefore, an urgent need exists to fill the knowledge gap in physiology, pathophysiology, and clinical management of patients with PFS.

Finasteride treatment impairs biosynthesis and function of neurosteroids, which are critical regulators of central (CNS) as well as peripheral nervous system functions and modulate a host of neurotransmitter receptors, such as gamma aminobutyric acid receptors. Thus, finasteride-induced neuroendocrine disruption of biosynthesis of critical signaling molecules results in pathophysiological states, which contribute to inhibition of biochemical pathways responsible for a host of physiological functions, ranging from sexual activity, mood, and cognition. In addition, finasteride-induced epigenetic changes in gene expression, including upregulation of androgen receptors (AR), increased histone acetylation, and methylation results in undesirable biological outcomes such as impairment of dopaminergic signaling and modulation of other neurotransmitter receptors, may be the underlying mechanism causing persistent or permanent adverse effects, manifested in anxiety, depression, and suicidal ideation.

The medical community has an obligation not to turn a blind eye on this rare yet debilitating condition in young men. Patients with this condition should not be stereotyped or

stigmatized by untrained and unprepared clinicians, due to lack of awareness and knowledge pertaining to this new and rare syndrome. Greater awareness and education is needed among the medical and scientific communities in order to develop better approaches for managing men with PFS. It is paramount that steps are taken to develop better understanding of the underlying mechanisms contributing to the onset and progression of PFS and to promote educational and training programs to increase awareness and improve management of this condition.