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Successful Finasteride Treatment Can Lead to Permanent Problems

By Petra Jungmayr

Editor's note: This English translation was done by a third party. The original German version can be accessed here.

In 2012, an increasing number of cases in the USA of sexual disorders that persisted even after discontinuing treatment with finasteride led to more stringent warnings about the side effects of the drug in its product information. Now, Merck faces a flood of lawsuits in the USA: Over 1000 men who suffer from the so-called Post-Finasteride Syndrome are demanding compensation for pain and suffering. In Germany the voices are also getting louder. But what is post-finasteride syndrome?

Post-finasteride syndrome consists of a long-term disorder of the sexual function as well as psychological and cognitive changes that occur during or after treatment of androgenetic alopecia with 1 mg Finasteride per day or during or after treatment of benign prostatic hyperplasia with 5 mg Finasteride per day. Most of these symptoms disappear after stopping the drug, but a small portion of patients suffer from persistent side effects such as sexual dysfunction, depression, anxiety, cognitive disorders, and a severe reduction in quality of life.

Post-Finasteride Syndrome - One Case

A case report describes a 24-year-old man with androgenetic alopecia and a rapid development of post-finasteride syndrome consisting of loss of libido, erectile dysfunction, and depression that began within two to five days of starting 1 mg finasteride. He stopped taking the drug approximately after one month but the symptoms persisted after discontinuation and remained unchanged for the next 11 years. The usual endocrinological serum parameters were in the normal range. The antidepressants used, as well as other drugs like sildenafil, were not effective or only marginally effective and were ultimately discontinued due to side effects [source: Kuhl H, et al.]

Irreversible blockade of 5α-reductase

The effects of finasteride are based on a sharp drop in 5α-dihydrotestosterone concentration due to an irreversible blockade of 5α-reductase to sexual organs, the brain, skin, and other organs and tissue types. This prevents the conversion of testosterone into the stronger androgen: dihydrotestosterone. Furthermore, the formation of neuroactive steroids such as 3α, 5α-pregnanolone (allopregnanolone), or androsterone is blocked (see Fig.). Absence of the sedative, antidepressant, and anxiolytic effects of these steroids in the central nervous system leads to a disturbed regulation of neuronal activity, which sometimes can lead to serious psychological and cognitive symptoms (Tab). In most cases, dihydrotestosterone concentration rises again after stopping finasteride due to new synthesis of 5α-reductase. However, in a small number of patients, the activity of 5α-reductase remains permanently inhibited. The cause of these irreversible changes is not clear; epigenetic processes may play a role in this.

Specific information on the frequency of post-finasteride syndrome cases is not available. Between 1998 and 2013, almost 5,000 spontaneous reports were received on an Internet platform set up by the National Institutes of Health, which specifically listed sexual dysfunction as a result of finasteride treatment. 11.8% of the cases were serious persistent disorders, some of which were associated with the risk of suicide. An estimation of how high the incidence of post-finasteride syndrome is cannot be derived from this. There is information about a

presumably low frequency of cases; but according to some authors, a high number of unreported cases may be expected.

No recommendations regarding therapy

There are currently no satisfactory treatment options for post-finasteride syndrome. Transdermal substitution of dihydrotestosterone led to an improvement in sexual symptoms in two placebo-controlled studies. However, cognitive functions, depression, and quality of life were not improved. When prescribing antidepressants, the advantages and disadvantages must be carefully weighed, as some antidepressants may improve the symptoms of depression but have an unfavorable effect on sexual function. Dopaminergic agonists such as bupropion may be more suitable. However, general recommendations are not available.

Public perception

Reports and information on post-finasteride syndrome can be found both in public media outlets (e.g. in “Die Zeit”, on “Spiegel online,” in Internet forums) as well as in specialist circles. For example, due to a growing public interest, the PFS Foundation was founded in 2012. It aims to educate doctors, scientists, and health organizations about post-finasteride syndrome.

In 2015, post-finasteride syndrome was registered in the U.S. National Institutes of Health, in the Genetic and Rare Disease Information Center. As part of the Research Portfolio Online Reporting Tool (RePORT), The National Institutes of Health listed an epidemiological study to document adverse effects of taking 5α-reductase inhibitors.

Tab: Influence of steroids and other substances on the GABA interaction with the GABAA receptor and its effect on the CNS [according to Kuhl H (Hrsg): Sexualhormone und Psyche, Thieme-Verlag Stuttgart 2002]

Substance	Influence on the activity of GABA on the GABAA receptor	Effect on the CNS
Estradiol	no effect	activating
Progesterone	no effect	inhibiting
Synthetic progestins	no effect	inhibiting
Testosterone	no effect	activating
Androstenedione	no effect	activating
11-deoxycorticosterone	no effect	activating
3α, 5α-pregnanolone (allopregnanolone)	increase	inhibiting
3α, 5β-Pregnanolone (Pregnanolone)	increase	inhibiting
3β, 5α-pregnanolone (isopregnanolone)	decrease	activating
3β, 5β-pregnanolone (epipregnanolone)	decrease	activating
Androsterone	increase	inhibiting

3α, 5α-androstandiol	increase	inhibiting
3α, 5α-tetrahydro-deoxycorticosterone	increase	inhibiting
Corticosterone	decrease	activating
Pregnenolone	decrease	activating
Dehydroepiandrosterone	decrease	activating
Benzodiazepines	increase	inhibiting
Barbiturates	increase	inhibiting
Ethanol	increase	inhibiting
Melatonin	increase	inhibiting

The influence on the activity of GABA is based on a positive or negative modulation of the GABAA receptor
GABA = γ-aminobutyric acid (γ-aminobutyric acid)

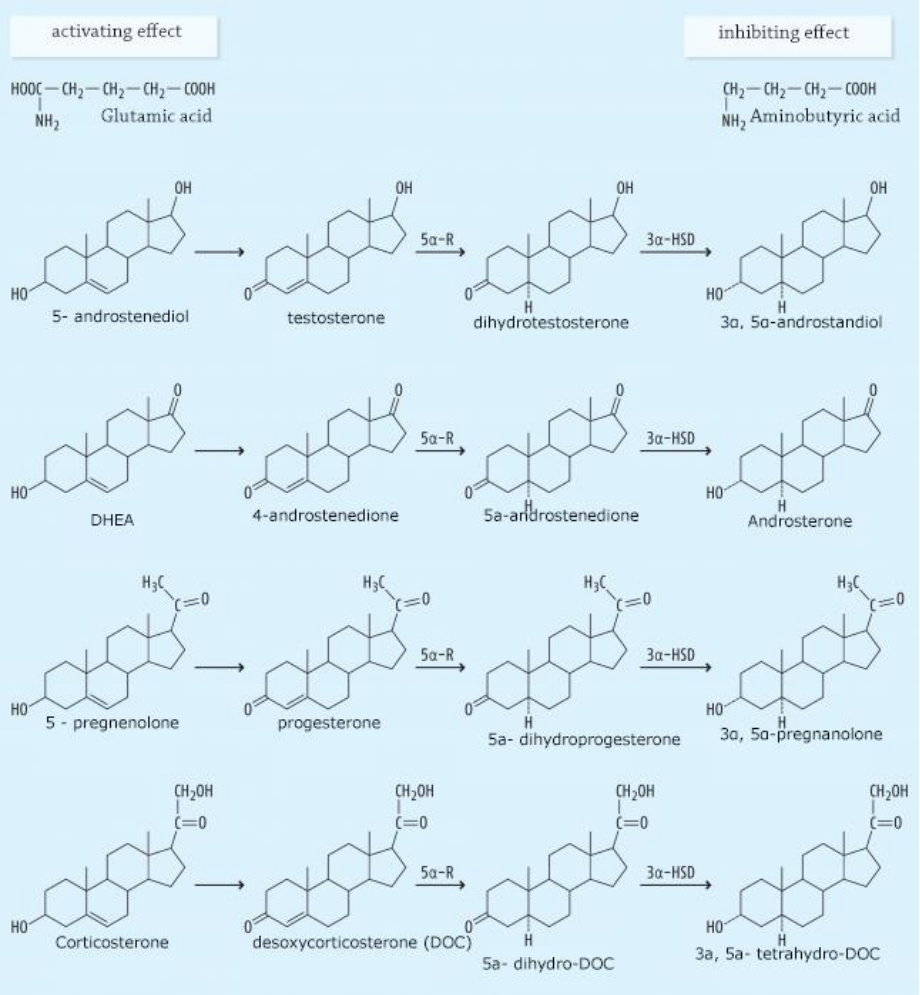

Fig: Neurosteroids. Steroids and their metabolites can influence neurotransmitter metabolism by modulating the GABA receptor via gamma-amino-butyric acid (GABA) in the central nervous system. (See table). The activating neurosteroids: 5-androstenediol, dehydroepiandrosterone (DHEA), 5-pregnenolone, and corticosterone are reduced to neurosteroids with inhibiting effects via 5alpha-reductase [source: Kuhl H, et al.]

Literature

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