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Post-Finasteride Syndrome (PFS) Update: Point/Counterpoint

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At the ISHRS 2015 Annual Scientific Meeting in Chicago, we heard an update on the constellation of symptoms that has come to be known as Post-Finasteride Syndrome (PFS). The update was presented by guest speaker Dr. Mohit Khera, Associate Professor in the Department of Urology at Baylor College of Medicine where he specializes in male infertility and sexual medicine. Based on the Audience Response System responses of those attending, it was obvious that his presentation influenced the audience's practice opinion toward finasteride. As a speaker and panel member, I am concerned that the format of the session did not allow for clarification of some of the unsubstantiated conclusions that were made in Dr. Khera's presentation, and did not allow for a complete discussion of all potential conflicts of interest (COI) he may have had concerning the topic. Furthermore, a counterpoint discussion with the audience was not taken.

Dr. Khera did mention a COI, that his study was funded by a grant from the Post-Finasteride Syndrome Foundation. This foundation was started by two physicians whose son developed severe depression during a period in his life when he had also taken finasteride. Their website describes the organization's focus to increase global awareness of the "devastating and life-altering impact finasteride can have on the sexual, mental, and physical health of men." While there are a number of clinician and research members, including Dr. Khera, of the International Society of Sexual Medicine and Sexual Medicine Society of North America who have strong opinions that PFS is a real entity, no studies to date have established that PFS is an actual entity, defined the at-risk patient population, or noted the actual incidence or the mechanism that could explain persistent symptoms. He referenced the often quoted publications of Dr. Michael Irwig, which have been heavily criticized for a patient database obtained from a website with a strong bias. Conclusions from his "studies," which have extreme selection bias and lack scientific controls, should be regarded with skepticism. Additionally, Dr. Khera is an Associate Editor of *The Journal of Sexual Medicine,* which has published several of these and related publications.

Beyond the above issues, I wish to address several points in Dr. Khera's presentation: male breast tissue, infertility, and prostate cancer.

Gynecomastia is a well-documented adverse event reported in up to 2% of men taking 5-alpha reductase inhibitors (ARIs). Dr. Khera raised an alarm concerning male breast cancer quoting a study in which 4 out of 1,554 men taking finasteride developed breast cancer, 200 times the general population. In my review of finasteride and dutasteride double-blinded, controlled studies of 28,000 men taking finasteride vs. placebo, 8 cases of breast cancer were reported, of which 3 were taking finasteride and 5 placebo. Of 22,400 men taking dutasteride vs. placebo, 3 cases of breast cancer were reported, 2 with dutasteride and 1 placebo. Based on these two large cohort studies, there is no statistical evidence to arrive at the conclusion of an increased incidence of breast cancer in men using 5 ARIs. While the patient information packets for finasteride and dutasteride mention post marketing associations with breast cancer, 50 cases have been reported in the world's literature, and 26 developed in less than a year within starting finasteride.

The Million Women Study in the United Kingdom was set up to investigate the effects of specific types of HRT [hormone replacement therapy] on incident and fatal of breast cancer.[1] It concluded that the risk of breast cancer increased with increasing total duration of HRT use. The report in men of so many cases within one year of starting the drug suggests that the cancers were not induced by finasteride. These cancers were already present and detected due to early discovery.

A review of this issue in the November 2013 *Journal of Urology* concluded that "the lack of an association suggests that the development of breast cancer should not influence the prescribing of 5 ARI therapy."[2]

During the Q&A session, Dr. Khera recommended against using finasteride in couples attempting conception. While his expertise is in infertility, there is ample data to support the opposite opinion that there is insufficient finasteride in normal ejaculate volume to adversely affect a potentially pregnant woman, or to reduce spermatogenesis or infertility in healthy men chronically taking finasteride.[3] The few studies with small populations implicating a reduction in male fertility appear to be in subfertile men or those with an underlying condition such as varicocele.[4]

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PFS Update *from front page*

Attendees may have left with the impression that 5 ARI cause high-grade prostate cancer. The original Prostate Cancer Prevention Trial (PCPT) study found a higher percentage of high-grade prostate cancer in men taking finasteride; however, subsequent analysis found multiple counter arguments against this increase being a real risk. Analysis of this same cohort 18 years later showed no significant difference between the two groups in rates of overall survival or survival after diagnosis of prostate cancer. Based on this information, it can be concluded that the increased Gleason scores initially noted were due to better detection by biopsy in prostates that were smaller from the effects of finasteride, and possibly increased sensitivity of PSA testing.

Since the approval of finasteride to treat androgenetic alopecia, the majority of members of the ISHRS have successfully helped thousands of patients. As physicians and clinicians, our primary concern is patient safety, and our desire is to discover the truth about this drug.

Placebo controlled clinical trials are needed to assess whether or not a causal link to finasteride exists as well as the incidence and possible etiology of central nervous system (CNS) and sexual side effects, and determining which patient populations may be at risk. The significant psychological aspects of potential side effects, magnified by sensationalized information on the internet and in the media, complicate the interpretation of data obtained outside of controlled, blinded scientific studies.

References

1. Beral, V., et al. Breast cancer and hormone-replacement therapy in the Million Women Study. *Lancet.* 2003(Aug 9); 362(9382):419-427.
2. Bird, S.T., et al. Male breast cancer and 5α-reductase inhibitors finasteride and dutasteride. *Journal of Urology.* 2013:190; 1811-1814.
3. Overstreet, J., et al. Chronic treatment with finasteride daily does not affect spermatogenesis or semen production in young men. *Journal of Urology.* 1999; 162:1295-1300.
4. Samplaski, M.K., et al. Finasteride use in the male infertility population: effects on semen and hormone parameters. *Fertility and Sterility.* 2013; 100(6):1542-1546.◆

On page 7 is Dr. Robert Bernstein's very comprehensive information sheet and consent form that he gives his patients. Most consent forms used by our colleagues are not this detailed. For that reason, we have also included the consent form used by Dr. Paul Rose in his office. Each one of us should choose a consent form with which we are comfortable and suits the laws of the country in which we live. —MM