

AEROMEDICAL IMPLICATIONS OF THE TREATMENT OF MALE HYPOGONADISM

CASE REPORT, BY JUSTIN B. NAST, MD, MPH

Male hypogonadism does not simply refer to the potential for testosterone deficiency that occurs with normal aging. Primary hypogonadism results from testicular disease and secondary hypogonadism results from disease of the hypothalamic-pituitary axis or lack of response to testosterone. This article presents a case report of a third-class pilot diagnosed with secondary hypogonadism that was being treated with clomiphene citrate.

History

A 35-YR-OLD MALE THIRD-CLASS pilot with nearly 300 hours' flying time was diagnosed with idiopathic secondary hypogonadism and was started on clomiphene citrate (Clomid), one 50 mg tablet three times per week. His medical history is significant only for right inguinal hernia repair and shoulder surgery. The airman was stable and without symptoms on this dose of clomiphene citrate (Clomid) when he applies for medical certification. He presents to his aviation medical examiner (AME) with a report from his treating physician.

Aeromedical Issues

The symptoms of untreated male hypogonadism with aeromedical implications include fatigue, sleep disturbances, anxiety, and depression (1). The general medical standards under Title 14 of the Code of Federal Regulations (CFR), parts 67.113, 67.213, and 67.313 indicate that the individual must have no organic, functional, or structural disease, defect, or limitation that would make them unable to safely exercise the privileges of their respective airman certificate. This regulation also states that any medication used to treat such a condition must not make the individual unable to safely perform the duties required of their certificate (2). The AME must make two determinations of the airman with male hypogonadism: Are the symptoms (whether treated or untreated) severe enough to preclude issuing a certificate? and are there any medications the airman is using to treat hypogonadism that are potentially unsafe for flying duties?

Testosterone therapy is a well-established, safe, and efficacious treatment for male hypogonadism. Potential side effects include skin irritation and a small risk of exacerbating prostate cancer (3). These side effects have no significant aeromedical implications, and an airman with hypogonadism that is being successfully treated with testosterone should be issued his certificate if there are no other disqualifying conditions.

Clomiphene citrate is a selective estrogen receptor modulator that has commonly been used to treat female infertility. It can also be used to treat male infertility in specific clinical scenarios (4). The use of Clomid in the treatment of male hypogonadism is an off-label use, but it has been shown to be both safe and effective for this purpose (5). According to the Guide for Aviation Medical Examiners, a medication is disqualifying if it has not been approved by the Food and Drug Administration to treat a particular medical condition (6). Because this airman

MALE HYPOGONADISM

Male hypogonadism is marked by low testosterone and low sperm count. Primary or hypergonadotropic hypogonadism is marked by above normal luteinizing hormone (LH) and follicle stimulating hormone (FSH). Secondary, or hypogonadotropic hypogonadism, is marked by normal or decreased levels of LH and FSH (9). Hypogonadism increases with age; the estimated prevalence is 39% in men over 45 (10). The most common causes of primary hypogonadism include genetic abnormalities, testicular trauma, mumps orchitis, and radiation/chemotherapy. Causes of secondary hypogonadism can also include genetic conditions, pituitary tumors, medications, and idiopathic cause. Mixed hypogonadism can be associated with systemic diseases such as liver failure, hemochromatosis, HIV, and chronic alcohol abuse (10).

is continuously using Clomid for the off-label treatment of hypogonadism, his application must be deferred to the FAA for disposition.

Outcome

The AME deferred the application to the Aeromedical Certification Division (AMCD). Initially, the AMCD granted a Special Issuance with the restriction of no flying 72 hours after each dose. This restriction was based on the normal dosing for Clomid when used to treat female infertility and included a 30-day limit.

The airman appealed this restriction because he would be unable to adhere to treatment three times per week and still be able to fly. Side effects of Clomid include hot flushes and mild abdominal discomfort occurring in less than 10% of patients. Visual disturbances have also been reported with Clomid use, and this does have aeromedical implications. There are conflicting cases in the literature regarding these visual disturbances, which can include persistent after-images (palinopsia), peripheral field distortion, and photophobia. An older study documented persistent changes in women undergoing infertility treatment,

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while a newer study found only very minimal changes that were insignificant and entirely reversible (7, 8). Because this airman had been stable on his current dose of Clomid with no visual changes for 12 months, he was granted a one-year time-limited certificate with no restrictions for the chronic use of Clomid, provided the dose not exceed 100 mg per day and he remains free of side effects.

Continued certification was contingent upon reporting any changes in the treatment regimen, and the AME would be able to reissue the time-limited certificate with a report from the treating physician.

References

1. Aydogan U, Aydogdu A, Akbulut H, et al. Increased frequency of anxiety, depression, quality of life and sexual life in young hypogonadotropic hypogonadal males and impacts of testosterone replacement therapy on these conditions. *Endocr J* 2012 Aug 31.
2. FAA. Guide for aviation medical examiners. Available online at: www.faa.gov/go/ameguide [cited 12/12/2012].
3. Lakshman KM, Basaria S. Safety and efficacy of testosterone gel in the treatment of male hypogonadism. *Clin Interv Aging* 2009;4:397-412.
4. Roth LW, Ryan AR, Meacham RB. Clomiphene citrate in the management of male infertility. *Semin Reprod Med* 2013 July;31(4):245-50.
5. Da Ros CT, Averbek MA. Twenty-five milligrams of clomiphene citrate presents positive effect on treatment of male testosterone deficiency — A prospective study. *Int Braz J Urol* 2012 Jul-Aug;38(4):512-8.
6. Silberman WS. Medications in civil aviation: What is acceptable and what is not? *Aviat Space Environ Med* 2003 Jan;74(1):85-6.
7. Purvin VA. Visual disturbance secondary to clomiphene citrate. *Arch Ophthalmol* 1995 Apr;113(4):482-4.
8. Racette L, Casson PR, Claman P, et al. An investigation of the visual disturbances experienced by patients on clomiphene citrate. *Fertil Steril* 2010 Mar 1;93(4):1169-72.
9. Pantalone KM, Faiman C. Male hypogonadism: More than just a low testosterone. *Cleve Clin J Med* 2012 Oct;79(10):717-25.
10. Dandona P, Rosenberg MT. A practical guide to male hypogonadism in the primary care setting. *Int J Clin Pract* 2010 May;64(6):682-96.



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