Treating Hypogonadism Due to Chronic Opiate Use: Walking the Slippery Slope of Iatrogenesis

Purpose: Explore the risks and benefits of treating hypogonadotrophic hypogonadism induced by chronic opiate use in a young man.

Learning Point: Evaluation of the known risks and benefits of testosterone replacement for hypogonadism

A 43 y.o. male with chronic low back pain secondary to a traumatic injury suffered years ago managed with high-dose opiate analgesia who also suffers from major depressive disorder and hypogonadotrophic hypogonadism presented to endocrine clinic on referral from his primary care provider (PCP) for evaluation of hypogonadism and recommendation for testosterone replacement therapy. The patient has a long history of fatigue, decreased libido, erectile dysfunction, insomnia and depression. 1 year prior to presentation, endocrine work-up revealed testosterone level of 88 (lower limit of normal 240) Luteinizing Hormone <0.1, Follicle Stimulating Hormone < 1.0 (both less than the lower limit of normal). At that time testosterone injections were initiated and continued for 6 months with improvement in his symptoms and testosterone level increasing to 975. Injections were then stopped when the patient experienced urinary retention and held until urology evaluation was obtained. Urology evaluation determined that lower urinary tract symptoms were likely due to chronic opiate medications and not obstruction from prostatic enlargement. With this evaluation and his improved symptoms on therapy, the patient was eager to resume testosterone therapy. His PCP explained the contribution of chronic opiate therapy to his hypogonadism and at the time of re-evaluation in endocrine clinic his opiate doses were being weaned down. Psychiatry evaluation determined his chronic pain is a major factor in his depression. He also noted mood swings with therapy. No changes were made in his mental health treatment regimen. During the most recent endocrine evaluation the patient was adamant that testosterone replacement resolved his symptoms and requested resumption of therapy. During discussion of adverse effects both known and theoretical he reported that he could no longer tolerate his symptoms and would accept any adverse effects or outcomes. Laboratory evaluation of pituitary function resulted in confirmation of diagnosis of hypogonadotrophic hypogonadism without effect on other pituitary dysfunction and the patient was started on testosterone replacement with gel in an attempt to mitigate mood swings. There have been no follow-up visits to determine effectiveness of treatment at this time.

Chronic opiate therapy suppresses the hypothalamus-pituitary-gonadal axis primarily through decreased Gonadotropin Releasing Hormone (GnRH) binding mediated by hypothalamic opioid receptors. In addition opioids exhibit direct effect on the testes through decreased sperm production and decreased intra-testes testosterone production.¹ These effects result in decreased testosterone levels and the clinical symptoms of sexual...

dysfunction, decreased libido, and infertility\textsuperscript{2}. While this effect on testosterone invites the thought of hormone replacement as an intervention, review of the literature does not support use of testosterone for this indication. Additionally, the adverse effects of testosterone replacement have not been well quantified, particularly in younger men. Known adverse effects include polycythemia, gynecomastia, acne, sleep apnea and infertility.\textsuperscript{3} Data is controversial regarding other adverse effects such as cardiovascular risk and some studies indicate decreased risk with treatment\textsuperscript{4} while a study of testosterone effect on older men with impaired mobility was stopped earlier for increased cardiovascular risk noted in the treatment group.\textsuperscript{5}

As physicians our desire is to mitigate our patients’ burden of disease yet it is our responsibility to fulfill this desire using the knowledge of our training and the guidance of clinical evidence. This case is complicated through the combination of a patient suffering symptoms that limit his ability to function, his conviction that these symptoms are relieved by testosterone replacement, and the confounding effects of depression and opiate analgesia on his presentation. Further, there is a paucity of data to guide his treatment, placing an additional burden on the physician when determining treatment options. With the recent experience of hormone replacement therapy in women and the suggestion of increased cardiovascular risk in men receiving testosterone replacement perhaps the wisest course of action it to recall our first duty and to avoid harming this patient with unproven therapy and to instead abate his suffering by directing treatment at the underlying causes.

\textsuperscript{2} Brennan, Michael J. \textit{The Effect of Opioid Therapy on Endocrine Function}. The American Journal of Science. 2013 126 s12-s18.


\textsuperscript{4} Ibid