Testosterone Replacement Therapies

TREATMENT OPTIONS FOR PATIENTS DIAGNOSED WITH HYPOGONADISM - PART II

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As noted in Part I of this series, endocrine suppression, or hypogonadism, is well documented to arise from: opiate therapy for chronic pain, aging, diabetes, and obesity. In recent years, increased focus on anti-aging and treatment of the whole patient has resulted in better patient outcomes and improved quality of life for hypogonadal patients. This is Part II of a two-part series on treatment options for hypogonadal patients. Part I focused on the identification and benefits of treating hypogonadism. Part II will focus on the side effects and issues associated with several Testosterone Replacement Therapies (TRT).

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When identified, hypogonadism is typically treated with one of several hormone replacement therapies. In males, hypogonadism is treated with Testosterone Replacement Therapy, or TRT. Compliance, diversion, and side effects are common complaints with oral, transdermal, and transmucosal routes of administration. Additionally, TRT via gels and foam preparations can be associated with virilization.

TRT via implantable pellet therapy provides a significant improvement in hormone replacement therapy for men. This type of technology avoids compliance and diversion issues associated with prescribed formulations. Additionally, increased compliance results in steady state Testosterone (T) levels and significant improvement in quality of life for chronic pain patients suffering from hypogonadism.

TREATMENT OF HYPOGONADISM

The use of Testosterone Replacement Therapy (TRT) in hypogonadal men has been well documented. Restoration of serum T concentrations to within normal limits can maintain sexual characteristics, sexual behavior, energy, mood, and muscle development and improve bone density.[1]

Testosterone is a Class III prescription drug available in gel (AndroGel® - Solvay and Testim® - Auxilium), transdermal patches (Testoderm, Androderm and Testoderm TTS), compounded gels and creams, transmucosal preparations, oral medications, intramuscular injections, and compounded implantable pellet technology.

TRT is available in many formulations and routes of administration, but many of these formulations have limitations. Orally available TRT formulations are suboptimal due to the relative insolubility of testosterone and high first pass effect in the liver. The skin and oral mucosa are considered a more favorable route vs. oral formulations; however, it can result in increased skin irritation, virilization, and variable compliance (both over dosage and under dosage).

In the aging population, skin irritation and skin breakdown may cause additional complications with transdermal formulations. Skin tolerability problems or the need for shaving large areas of scrotal skin invariably affect compliance with transdermal patches. Skin reactions commonly occur at the patch application site, particularly with the permeation-enhanced T patches causing erythema or pruritis. Blister reactions leading to scarring and discontinuation of treatment have also been reported.

Gels and foams appear to be less irritating to the skin vs. patches; however, there is an increased risk of virilization and transfer onto clothing, due to lack of proper hand washing after application. Dosing/compliance can also be an issue.

TRT is also available as an intramuscular injection. Intramuscular injections have been reported to result in wide fluctuations in T levels. Specifically, high initial peak levels, followed by serum T levels below the lower limit of normal toward to the end of the cycle leading to a return of clinical signs and symptoms of hypogonadism.[1]

It is postulated that implantable pellet therapy is an optimal route of administration due to improved compliance, decreased dosing variability, reduction in skin irritation, improved clinician control, and

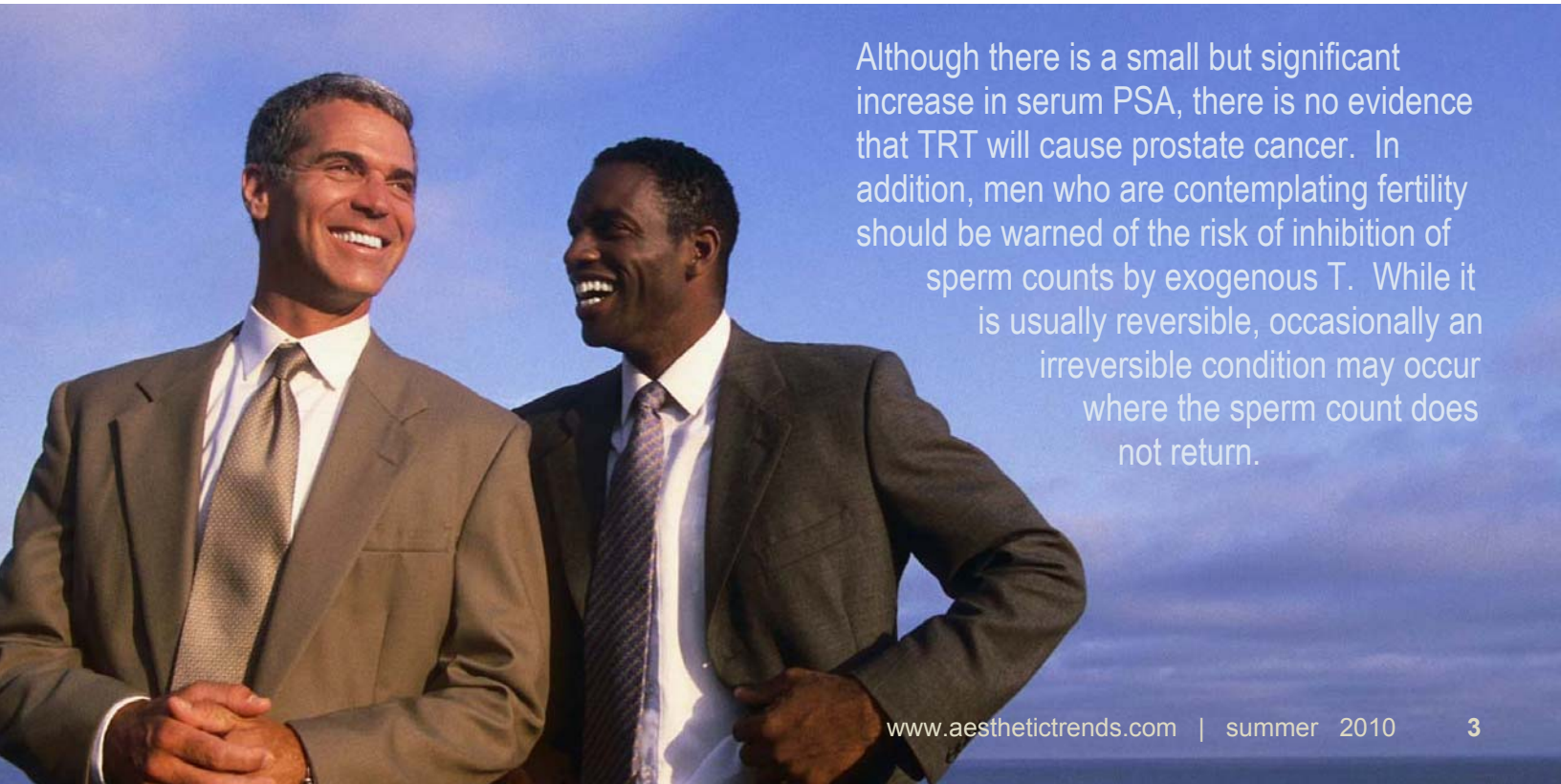
lack of risk of diversion while attaining optimal therapeutic outcomes.

The procedure for implanting TRT pellet therapy is fairly simple. The area of implantation is sterilized and anesthetized. A torchar is introduced through a small incision, and the pellets are placed into subcutaneous fat. The incision is then stitched and secured with a butterfly bandage/sterigauze. Patients should refrain from showering for 24 hours or swimming for 72 hours.

Among the most valuable benefits of pellet therapies to both patient and physician is the ease of compliance with reduced risk of dosage variation once the patient has been properly titrated and stabilized. This characteristic allows enhanced efficacy of treatment, ultimately leading to better quality of life through disappearance of symptoms related to hypogonadism.

POSSIBLE RISKS ASSOCIATED WITH TRT[2]

- Polycythemia (more common in IM injections and/or smokers)
- Increased PSA (BPH and prostate cancer)
- Edema in patients with or without pre-existing cardiac, renal, or hepatic disease
- Precipitation or worsening of sleep apnea
- Acne
- Decrease in testicular size and/or sperm count /Infertility
- Gynecomastia - more common in IM injections
- Hepatotoxicity (with oral therapy) (increase in liver enzymes, cholestasis, and hepatic tumors)
- Hypertension



Although there is a small but significant increase in serum PSA, there is no evidence that TRT will cause prostate cancer. In addition, men who are contemplating fertility should be warned of the risk of inhibition of sperm counts by exogenous T. While it is usually reversible, occasionally an irreversible condition may occur where the sperm count does not return.

IN CONCLUSION

Male chronic pain, diabetic, obese, and elderly patients are at a significantly high risk for hypogonadism. TRT has been proven to restore testosterone levels to normal levels in hypogonadal males.

The benefit of normalized testosterone levels includes improved quality of life, increased libido and sexual function, improved body composition and muscle mass, and decreased risk for osteoporosis.

It is important to carefully screen male patients prior to the initiation of TRT. Increased PSA levels and a high risk for breast or prostate cancer are contraindications to therapy. TRT is available in many different forms and routes of administration. However, oral, transdermal, transmucosal, and intramuscular injection formulations, although effective, carry limitations to therapy.

TRT via implantable pellet therapy appears to reduce the inconvenience, multiple side effects, and likelihood of diversion associated with other formulations. Implantable pellet technology results in a great advancement for an undertreated population. TRT administered via implanted pellet technology will result in greater patient compliance, improved steady state T levels, and improved long-term therapeutic results while keeping the risk of diversion and possible side effects to a minimum.

References

1) Brawer, M. Reviews in Urology Vol 6, Supp 6, 2004; pgs. S9-S15.

2) Steidle, C. , Schwartz, S., Jacoby, T., Sebree, T., Smith, R., AA2500 Testosterone Gel Normalizes Androgen Levels in Aging Males with Improvements in Body Composition and Sexual Function, *The Journal of Clinical Endocrinology & Metabolism* 88(6): 2673-2681.

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