



Platinum Priority – Editorial

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Is a Normal Testosterone Level Necessary for Erectile Function?

Taylor P. Kohn^a, Ranjith Ramasamy^{b,*}

^a Baylor College of Medicine, Houston, TX, USA; ^b Department of Urology, University of Miami Miller School of Medicine, Miami, FL, USA

Erectile dysfunction is defined as the inability to achieve or maintain an erection that is satisfactory for sexual performance [1]. Vascular, neurological, psychological, and hormonal factors are all involved in initiating and maintaining an erection. Of these, the hormonal factor is the easiest to assess by measuring morning testosterone levels. The association between erectile dysfunction and testosterone levels is well documented in the literature. The European Association of Urology (EAU) guidelines for the diagnosis of erectile dysfunction recommend assessing total testosterone levels [2].

In this issue of *European Urology*, Corona et al [3] report findings from a meta-analysis of 14 randomized controlled trials that measured the effect of testosterone therapy on erectile function, as assessed by the International Index of Erectile Function-Erectile Function Domain (IIEF-EFD). They demonstrate that compared to placebo treatment, testosterone therapy provides only modest improvement in IIEF-EFD (a mean difference of 2.31 points). When stratified by baseline testosterone level, they found a greater improvement in erectile function for men with severe hypogonadism. In primary studies with an inclusion criterion of testosterone <8 nM (231 ng/dl), the IIEF-EFD score increased by 2.95 points, whereas in primary studies with an inclusion criterion of testosterone <12 nM (346 ng/dl), only a 1.47-point increase in IIEF-EFD score was observed [3]. This greater improvement among men with severe hypogonadism supports the theory that once the threshold of a “normal” testosterone level is achieved, additional testosterone therapy does not further improve erectile function [4].

The improvement in erectile function due to testosterone therapy may be enzymatically linked to phosphodiesterase type 5 (PDE5). Several animal studies demonstrated that testosterone regulates both nitric oxide and PDE5

levels, which are both essential for erectile function [5]. Potentially, men with hypogonadism may have a relative deficiency of the PDE5 enzyme, lowering the efficacy of PDE5 inhibitors [6]. In a randomized controlled trial by Shabsigh et al [7], dual treatment with sildenafil and testosterone was more effective than monotherapy with sildenafil for men with testosterone <400 ng/dl who had previously failed a trial of a PDE5 inhibitor. While additional research is still required to elucidate the relationship between testosterone and PDE5, the evidence supporting testosterone use in men with low testosterone and mild erectile dysfunction is strong [3,8].

The findings by Corona et al suggest that testosterone therapy may only be useful in improving erectile function in men with mild erectile dysfunction. If testosterone therapy can obviate the need for PDE5 inhibitors or improve the response to PDE5 inhibitors, then testosterone therapy has a unique and beneficial role in the treatment of these patients. We postulate that testosterone monotherapy may not be as useful in men with moderate and severe erectile dysfunction, as the etiology of more severe erectile dysfunction may include pathologies such as advanced diabetes, radical pelvic surgery, or severe neurological damage. For these men, alternate erectile therapies may be more effective.

Conflicts of interest: The authors have nothing to disclose.

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* Corresponding author. Department of Urology, University of Miami Miller School of Medicine, 1120 NW 14th Street, Miami, FL 33136, USA. Tel. +1 305 2436090.

E-mail address: ramasamy@miami.edu (R. Ramasamy).

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