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Review

Outcomes of testosterone therapy in men with testosterone deficiency (TD): Part II

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ABSTRACT

Testosterone (T) deficiency (TD) is a common clinical condition, which contributes to co-morbidities including loss of muscle mass, increased fat mass, increased inflammation, insulin resistance, risk of vascular disease, sexual dysfunction, fatigue, depressed mood and reduced quality of life. T therapy attenuates inflammation, increases insulin sensitivity, muscle mass and reduces fat mass and adiposity. T therapy improves lipid profiles and endothelial function and reduces systolic and diastolic blood pressure. In addition, T therapy may reduce risk of vascular disease and mortality. T therapy improves bone mineral density and increases energy and vitality and improves mood and sexual function and overall quality of life. T therapy appears to be safe if treatment and monitoring are appropriately executed. The evidence available to date does not support alleged concerns regarding risk of cardiovascular disease and prostate cancer. Indeed, T therapy remains controversial. The data in the contemporary literature suggest that T therapy reduces cardiovascular risk and fears promoted by some recent studies should be re-evaluated. The cardiovascular risk and mortality with T therapy must await large prospective controlled clinical trials, which depend on many complex factors. Such studies may be prohibitive in the current environment due to logistical challenges, such as recruiting large number of men to be treated for long-durations with appropriate follow-up, requiring astronomical cost.

Contents

1. Introduction

We have presented a comprehensive discussion of the adverse effects of TD on men's health [1]. In this review we focus on presenting and discussing the contemporary data from the literature

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on the positive impact of T therapy on overall health and quality of life, in men with TD. As far back as 1940, T therapy in men with TD, when given at the physiological range, was deemed beneficial to overall health and had no demonstrable side effects [2,3]. These early observations pointed out that if T treatment was in the physiological range, no harm of T therapy was noted [2,3]. Over the past seven decades a large number of studies were published on T therapy in men with TD. While some of these studies had small number of patients, or were of short duration and others may have been observational in nature, many of these studies have provided a wealth of information on the improvement in the overall health of men with TD. In this review, we summarize data from long-term, cumulative, uncontrolled, observational registry studies demonstrating that T therapy restored physiological T levels within the first 12 months and T levels were maintained with T therapy throughout the entire study period [4–8] with positive beneficial effects on body weight (weight loss; WL), waist circumference (WC), body mass index (BMI), lipid profiles and inflammatory biomarkers. The summary of the findings are outlined in Fig 1. T therapy in men improves insulin sensitivity, lipid profiles, endothelial function and may reduce the risk of cardiovascular disease and mortality. T therapy demonstrated significant reduction in fasting blood glucose, HbA_{1c}, WL, WC and BMI and improvement in lipid profiles, sexual function and quality of life.

2. T therapy reduces inflammatory biomarkers in men with TD

TD is associated with increased expression of inflammatory cytokines [1]. Epidemiological, observational, and interventional studies showed that T levels are inversely correlated with inflammatory biomarkers such as high sensitivity C-reactive protein (hs-CRP), liver function enzymes, IL-1β, TNF-α, and IL-6 [9–12]. Recently, we have reported that T therapy reduces activities of liver enzymes and reduces C-reactive protein (CRP) levels in obese and diabetic men with TD, suggesting attenuation of the inflammatory response and improvement in various physiological functions [4–8]. These findings strongly suggest that normalizing physiological T levels in men with TD ameliorates metabolic syndrome (MetS) components and reduces inflammation [4–8]. As shown in Fig. 2, long-term T therapy in men with TD markedly and significantly reduced CRP levels, suggesting T therapy reduces inflammatory responses. CRP concentrations were thought to be significantly associated with change in systolic blood pressure (SBP) and WC and inversely associated with HDL levels [13]. T therapy improved both systolic and diastolic blood pressure and reduced WC in men with TD. It is likely that such changes in metabolic function contributed to the reduction in CRP levels observed in the long-term treatment studies [4–8,13]. More interestingly, Schnell et al. [14] suggested that treatments which reduce inflammation as assessed by CRP levels are associated with reductions in HbA_{1c} in diabetic individuals. We have noted that T therapy produced significant and sustained reduction in HbA_{1c}, suggesting that normalizing T levels reduces inflammation and restores glycemic control [8].

3. T therapy improves insulin sensitivity and reduces glucose and HbA_{1c} levels

A number of studies have shown that T therapy elicits positive effects on blood glucose levels, insulin sensitivity, and reduction in glycated hemoglobin (HbA_{1c}) levels [15–28]. T therapy produced marked decrease in fasting blood glucose and HbA_{1c}, suggesting that T therapy ameliorates hyperglycemia and insulin resistance

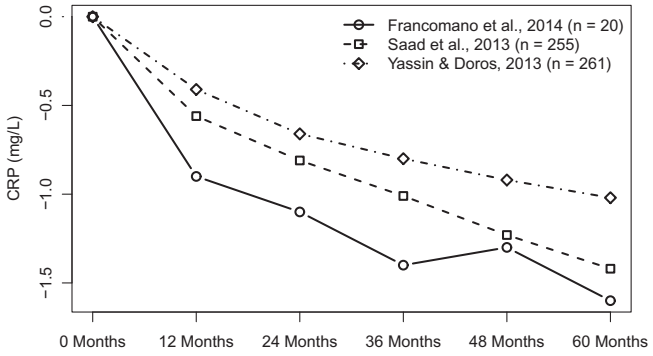

Fig. 2. Effects of long-term T therapy on CRP levels in men with TD. T therapy results in marked and progressive reduction in CRP levels. Data were derived from observational studies from three independent clinical centers. The data were obtained from the observational registry studies reported by Saad et al. [4], Haider et al. [5,6], Traish et al. [8], Yassin and Doros [7], and Francomano et al. [15].

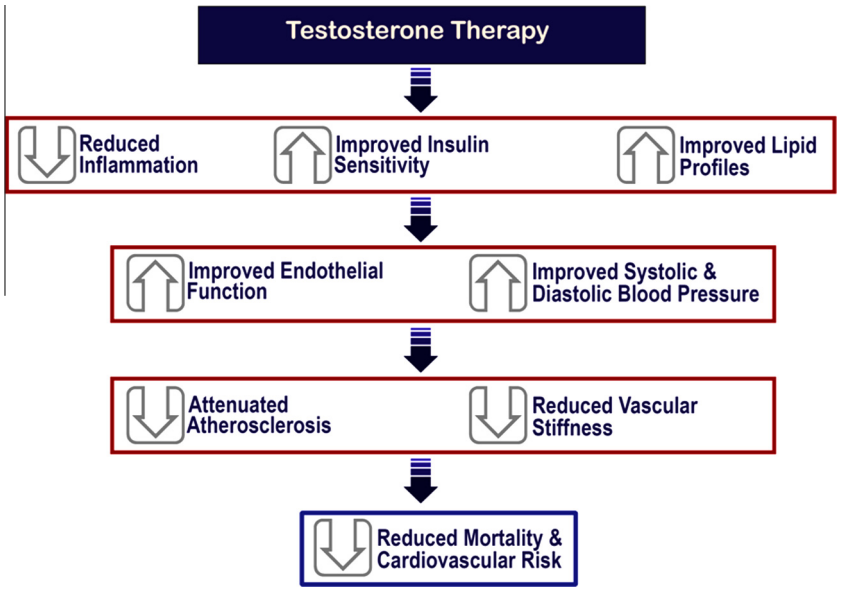

Fig. 1. Effects of T therapy on physiological and metabolic function in men.