Short Communication

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Low Testosterone Level and Metabolic Syndrome, Obesity, Diabetes

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ABSTRACT

The effects of testosterone include sex differentiation, muscle formation, increase in bone density, promotion of erythropoiesis, erectile function, etc. With aging, the concentration of testosterone in serum decreases at a rate of 0.4-2.6% per year. Hypo testosterone is a well-studied disease, and the deficiency is defined as a clinical syndrome associated with increasing age and comorbidities. It is characterized by the level of testosterone in the blood and its correlation with other complicated conditions. Low testosterone is defined by a value <350 ng/dL (12nmol/L). The low level of testosterone will have adverse effects on multiple organs of the body, leading to a decline in the quality of life, including change in sexual function, apparent obesity (men with low testosterone and women with excessive testosterone), abdominal obesity (indicated by excessive waist circumference and other potential metabolic and cardiovascular diseases. Patients of chronic diseases may sometimes suffer with relatively lower concentration of testosterone in their blood, especially showing related symptoms like osteoporosis, erectile dysfunction, metabolic syndrome, etc., as well as abnormal body fat distribution and insulin resistance.

Keywords: Metabolic Syndrome; Cardiovascular Risk; Testosterone Replacement Therapy; Blood Testosterone Concentration; Obesity in the Elderly

Introduction

According to studies, men over age of 45 can develop hypogonadism and the rate of insufficient testosterone concentration is as high as 38.7% [1]. The low level of testosterone can be specified as degree of testosterone deficiency, ranging from mild to severe, showing signs of low libido, lack of vitality, fatigue, mood changes, insomnia, anemia, delayed ejaculation, flushing, erectile dysfunction, muscle atrophy, and fat accumulation in the abdominal cavity. Other symptoms may also include testicular atrophy, general weakness, insufficient bone mass (osteoporosis), and hair loss on the face, underarms, and perineum. Risk factors like (1) seniority, (2) obesity, and (3) diabetes is all related to decreased concentration of blood testosterone.

The low level of testosterone due to obesity and diabetes can often categorized as primary (testicular hypofunction) and secondary (pituitary hypofunction), affecting two organs and implying a bidirectional influence on each other [2]. Common acquired causes of the primary type of the disease are age (such as the menopause) and long-term use of specific drugs that interfere with testosterone synthesis (such as the myco inhibitor, Ketoconazole; the immunosuppressant, Cyclosporin; and the chemotherapy drug, Cisplatin). Other causes may include mump infection, orchiditis, testicular trauma, testicular torsion, orchiectomy, and factors like radiation damage, environmental poison, etc., all of which lead to decreased production of testosterone by the testicles [3]. On the other hand, trauma to the pituitary gland, hemorrhage, and even brain tumors and brain metastases of other malignant tumors are one of the common causes of acquired secondary hypogonadism [4]. The low concentration of testosterone in the blood of obese patients is related to hypertrophy and dysfunction of adipocytes.

Low testosterone is known to cause many chronic diseases, such as Leptin resistance: fat cells secreting leptin to cause leptin resistance in the center and reduce the kisspeptin signal in the hypothalamus that in turn reduces GnRH (gonadotropin releasing hormone) and Luteinizing hormone (LH) secretion, where the Leydig cells of the testis interfere with LH action and further reduce the testosterone production; Estrogen action: adipocyte aromatase enzyme (aromatase enzyme-CYP19A1) catalyzes the conversion of androstenedione and testosterone into estrone (E1) and estradiol (E2), which negatively feedback on the hypothalamic-pituitary pathway to reduce the production of testosterone; and Proinflammatory cytokines: Fat cells produce more tumor necrosis factor-α (TNF-α), interleukin-1 (interleukin, IL-1) and interleukin-6, as these cytokines start interfering with the kisspeptin signal in the hypothalamus and reducing GnRH secretion, for which many studies also showed these to reduce the sensitivity to insulin, cause tissue inflammation, and produce insulin resistance [5,6].

Other conditions may also develop, like decreased muscle differentiation, increased tissue inflammation, decreased mitochondrial function, and affected lipoprotein lipolytic enzymes to produced free fatty acids for more fat accumulation in muscles, liver, and pancreas. These mechanisms are all contributing to reduced insulin sensitivity and associating the patient with the condition of insulin resistance. Hyperinsulinemia also reduces the kisspeptin signaling, leading to hypogonadism and hypo testosterone condition. Previous animal experiments on mice have found that mice with removed androgen receptors have increased fat accumulation, increased blood triglycerides and body weight, as they would also develop resistance to leptin and insulin [7]. The study found that testosterone supplement to obese men did reduce fat and improved lean body composition, as well as being associated with improved hemoglobin A1c and β-cell function[8]. The supplement is effective in reducing the total amount of fat and the effect is quite profound, which may be attributed to the fact that testosterone can inhibit lipoprotein lipase, regulate adipocyte differentiation, and reduce the distribution ratio of visceral fat. For an individual with obesity and severe symptoms of low testosterone (such as suffering from erectile dysfunction), testosterone supplement with weight loss exercise may improve symptoms significantly [9].

Testosterone, Obesity, and Insulin Resistance are Triad of Metabolic Syndrome

In summary, low testosterone, obesity, and insulin resistance are mutually correlated and may lead a person into a vicious cycle of deterioration. Low testosterone can also affect men's body composition, quality of life, emotional stability, bone density, and sexual dysfunction, while it is also known to increase cardiovascular disease risk. In the practice of weight loss clinics, medical history and symptom inquiries by adopting questionnaires such as the low male hormone assessment scale, AMS rating scale (Aging males symptoms rating scale) or ADAM questionnaire (Androgen Deficiency in Aging Men questionnaire ADAM) and body composition analysis (body Composition), as well as tests like sex hormone detection, and insulin resistance to screen obese or overweight patients with hypogonadism, all helped physician to find the most appropriate treatment regimen of testosterone supplement for these subjects to reduce insulin resistance that will improve their physical and mental health. It is worthy to note that blood is usually drawn between 7a.m. and 11a.m. when the blood testosterone concentration is the highest. If the blood testosterone concentration is lower than the target threshold and the patient shows symptoms, the case is immediately diagnosed as low testosterone [10,11].

Conclusion

Supplementing testosterone and adjusting daily life can help the elderly of low testosterone with or without obesity, particularly in the following areas: 1. Loss of muscle mass and hip BMD due to weight loss; 2. Improved aerobic capacity (increase peak oxygen consumption, VO2 peak), as an important indicator of the elderly to maintain independent lifestyle; and 3. Improved sexual function such as erection, orgasm, libido and sexual intercourse for more satisfaction with life; and 4. Restoration to normal testosterone level. Common symptoms of hypo testosterone syndrome include easy fatigue, decreased bone density, emotional instability, decreased activity and motor function, decreased muscle mass, decreased libido, sexual dysfunction, infertility, etc., but at a gradual pace of progression. The possible diseases and symptoms of low serum testosterone include obesity in 52% of reported cases (BMI > 30 kg/m^2), type 2 diabetes, long-term use of analgesic opioids in 53% of reported cases (74% with long-acting regimen), osteoporotic fractures and rapid weight loss. Clinically, if a male experiences sexual dysfunction and given the age as a sign of possible menopause, it is recommended to test the serum testosterone concentration to rule out hypo testosterone syndrome.

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