

Androgen Deficiency and the Efficacy of Replacement in Elderly Male Patients

¹Prof. Abdulrahman Alshaikh, ²Dr. Alshaymaa Abdulrahman Alshaikh,
³Dr. Hind Sajdi Alatawi., ⁴Dr. Arwa Meshal Alshaikh, ⁵Maged Mazen Fageeh,
⁶Mohammed Abdulrahman Alshaikh

King Abdulaziz university hospital medical department

Abstract: Aim: to review the efficacy and safety of androgen supplementation in symptomatic male patients.

Method: we reviewed patients with androgen deficiency with no pituitary or testicular disease. Patients with chronic diseases excluded. We followed the United State Androgen Replacement Society guidelines.

Results: One Hundred and Twenty three male patients above 60 years of age diagnosed to have androgen deficiency in endocrinology clinic at King Abdulaziz University hospital. Generalized body pain, fatigability and decrease sexual desire were the commonest complaints in those patients. The levels of testosterone were low with normal gonadotropins hormone. They treated by injection of long action testosterone. They improved clinically with no side effects been countered.

Conclusion: low androgen in healthy middle or old age is not uncommon. Treatment of androgen deficiency is mandatory which improve the wellbeing and relieves nearly all the symptoms. The safety needs more studies with large number and longer period.

Keywords: androgen, testosterone, elderly male patients.

1. INTRODUCTION

Both the absolute number and the proportion of men above age of 60 years of age will increase during the next 50 years.[1] Safe and effective medical interventions to promote healthy aging are therefore potentially valuable. Hormonal methods are promising because testosterone is inexpensive, and androgen has anabolic effects on muscle, fat and bone as well as muscle mass and strength, all of which are known determinants of physical function, disability, and quality of life.[2] The testosterone level may decrease by 1-2% annually in elderly men.[3,4] Benefit of testosterone treatment in such cases proved in some literature. In this study we reviewed 33, Male patients above 60 years of age with symptoms suggest of androgen deficiency, they treated by testosterone after checking the serum level. We noticed psychological and functional improvements.

2. PATIENTS AND RESULTS

All male patients with complaints suggest of androgen deficiency, like fatigability and decrease libido, undergo testosterone assessment after excluding other possible causes of their complaints. The patients with chronic medical illness should be excluded because it has similar symptoms such as diabetes, chronic renal failure, chronic liver disease, anemia, persistent heart failure, or other endocrine diseases. The clinical feature of androgen deficiency, I followed as suggested in various literatures, (see the discussion), including the following, fatigability, bone pain, arthralgia, and decrease libido. One Hundred twenty three male patients were diagnosed to have low testosterone level out of 189 male patients had blood test for testosterone level because the symptoms they has suggestive of androgen deficiency.

The ages of those patients diagnosed to have low testosterone level were above 60 years (61 – 83), with mean age of 67 years. Fatigability, bone pain and decrease libido were the mean feature in all of them, where sleeping more than usual and lack of interest in his work been found in less patients (table 1). Serum electrolytes, creatinine levels, liver enzymes,

and blood sugar levels were within normal levels. They treated by testosterone injection every 3 weeks. They showed improvement in their symptoms except one who continue to be symptomatic inspite of treatment for three months. The testosterone levels were normalize in all after 3 months of treatment.

3. DISCUSSION

Longitudinal studies indicate that key functional determinants, such as muscle strength and bone mineral density, decline by 1-2% and less than 1%/year between the fifth and ninth decades, respectively, and furthermore, that ageing is associated with increased fat, insulin resistance, falls and fractures, and decreased muscle mass, muscle strength, physical performance, bone mineral density, and libido.[5,6,7] These clinical feature, although individually nonspecific, are reminiscent of organic androgen deficiency when considered as a whole. However, determining whether aging is really a functional state of relative androgen deficiency and therefore potentially responsive to androgen therapy requires careful evaluation of efficacy and safety. Based on known androgen action, the greatest benefits lie in improvements in muscle, fat, and bone mass and function, whereas the greatest safety concerns arise from putative sleep – related, prostatic, and cardiovascular effects. Androgen supplements in older men with low or low normal serum level showed effects on muscles and fat.[8,9] There are no significant improvements in the muscles but the mild effects in the size enough to increase the strength by 3%.[10] Furthermore, it remains unclear whether such a small increase in muscle strength, which would be highly important for elite sportsmen, materially improves, daily living for frail older men.

Testosterone may improve insulin sensitivity, because T reduces intraabdominal fat mass, and low serum T levels predict the development of type 2 diabetes mellitus.[11,12]

The effect of exogenous androgenic enhancement on skeletal bone content in healthy older men appears to depend on androgen dose used, and the degree of baseline T deficiency.[13,14] The safety margin for testosterone use appears narrow particularly for injectable testosterone, but may be wider with more steady state preparations provided sufficient testosterone can be delivered.

Despite the equivocal benefits of androgen supplementation on muscular strength, physical function, and insulin sensitivity as well as fracture efficacy and bone mass, T prescription and use are increasing almost exclusively in the US.[15] Importantly, there is an increased prevalence of prostatic disease, cardiovascular disease and obstructive apnea with age. The likelihood that such male predominant diseases are androgen sensitive implies that even small detrimental effects of androgen on these end points in a large population at potential risk could negate any other modest benefits. Prostate disease, particularly cancer, and cardiovascular disease are the preeminent safety concerns. Androgen effects on cardiovascular outcome, even if minor or transient, could trump all other androgen actions.[16] The effect of androgen on cardiovascular risk is not known, because outcome – based data in men of any age are not available. However, short-term (<3months), randomized, placebo-controlled studies in middle aged men with coronary artery disease report some improvement in chest pain and objective responses to cardiac stress testing.[16] Inflammatory reaction and thrombosis markers may be improved with androgen supplementation. Furthermore, epidemiological associations' relative low, rather than high testosterone concentrations to cardiovascular morbidity.[17] Hence cardiovascular safety is less clear than ever, because the newly recognized benefits must weighed against the long presumed, but undemonstrated, concern that androgens may accelerate cardiovascular disease. A major unanswered question is whether androgen supplementation improves or worse cardiovascular outcome.

The idiosyncratic adverse effects of the testosterone should be considered. It has been documented that androgen worsen sleeping and breathing.[18] Androgen supplementation in high dose also exacerbates polycythemia, which may necessitate dose reduction.[19] Furthermore, the dose dependency of these adverse effects suggests that dose escalation to increase muscle, bone, or other efficacy will require careful evaluation.

A key lesson from the Heart and Estrogen/Progestin Replacement and Women's Health Initiative studies is that conventional medical practice should not precede substitution with reliable clinical evidence of safety and efficacy. Androgen replacement in older men is the male counterpart of hormone replacement therapy replacement in postmenopausal women, but differs crucially in that a clear syndrome of androgen deficiency is lacking, and conventional medical practice is still evolving. The increasing use of testosterone in healthy old men in the absence of considerable efficacy and safety concerns has promoted best – practice guidelines. These guidelines will continue to evolve as new information becomes available. Clinical features of androgen deficiency are non specific but necessary for diagnosis. Common markers are symptoms, such as lethargy, fatigability, diminished libido, depressive mood, and tiredness, and

signs, and signs such as reduced muscle and bone mass, increase visceral fat, impotence, and cognitive impairment. The Endocrine Society of Australia and the United States Endocrine Society have independently formulated similar recommendations for the biochemical of androgen deficiency in older men (figure 1).[20,21] Total testosterone concentrations of less than 200 ng/dl in the men in the U.S. (8nmol/l in Australia) and 200-400 ng/dl (9-15nmol/l) indicate overt and possible androgen deficiency, respectively. Concentrations greater than 400 nm/dl (15nmol/l) exclude androgen deficiency. Proper evaluation before commencing treatment requires a second confirmatory blood testosterone concentration. Determination of blood LH, FSH, and SHBG concentrations as well as bioavailability and free testosterone should be considered. Bioavailability and free testosterone may help clarify the clinical feature in men with symptoms and signs suggestive of androgen deficiency and border line total testosterone concentrations of 200-400 ng/dl, particularly in older age, because SHBG increase with age.

Androgen treatment should be monitored age appropriately. The diagnosis must be followed by specific appraisal and definition of the cause, which may include the hypothalamus, pituitary and/or testes (figure 1). It essential to confirm a normal digital prostatic examination and serum PSA, before therapy, and 3 months later after initiation of androgen treatment in men over age of 50 years. More research must be conducted to appropriately revise these guidelines. Our patients in this study did not showed any side effects of androgen therapy and showed improvement in there symptoms, mainly the fatigabilities and decrease libido. It is early and short study to confirm the safety of androgen supplementation. We need more studies with large number of patients and to be followed for longer period.

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