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Serum testosterone levels in South African men and the onset of androgen decline in ageing males

M. S. BORNMAN, M.B. CH.B., D.SC., M.D.
S. REIF, M.MED. (UROL.), F.C.S.A. (UROL.)
Department of Urology, University of Pretoria

Late-onset hypogonadism (LOH) in men is defined as 'a clinical and biochemical syndrome, associated with advancing age and characterised by typical symptoms and a deficiency in serum testosterone levels'.[1] Terms like 'male climacterium',[2] 'andropause',[3] or the 'male menopause'[4] are misnomers of the condition, and their use is outdated.[5] The testosterone deficiency may adversely affect the function of multiple organ systems and subsequently result in a significant loss of quality of life.[1]

Androgens are essential for the development and maintenance of male reproductive organs and male characteristics.[6] Testosterone is the major androgen and only 1 - 2% of serum testosterone occurs in the free form. The rest is bound[13] to sex hormone-binding globulin (SHBG) and albumin. Collectively, the free testosterone and albumin-bound fractions represent bio-available testosterone and more closely reflect the 'true' androgen status.[7,8]

In men, testosterone production is affected in a slowly progressive way after the age of 30 years,[9-11] as part of the normal ageing process. In elderly men, the circadian rhythm of testosterone is lost and the early-morning peak is lowered.[10,12] After 60 years, > 20% of men have subnormal testosterone levels and after 80 years, > 30% have subnormal levels.[7,9] Between 25 and 75 years, the major decline occurs in the total serum testosterone (~30%);[11,12] however, the decline in bio-available testosterone and free testosterone of ~50% is due to the age-associated increase in SHBG binding capacity.[13] Acute or chronic illness, physical/psychological stress, surgery, substance abuse, etc. may accentuate the symptoms of age-associated testosterone decrease.[5,14]

The symptoms of LOH are nonspecific and usually develop in a slow progressive way over a relatively long period of time, making their appearance hardly perceptible. Mood changes are often the first to appear, but sexual and erectile symptoms are usually the complaints that will bring the patient to the physician. Body and visceral fat mass increase, inducing a higher risk of insulin resistance, type II diabetes mellitus, cardiovascular disease, osteoporosis, or even osteoporotic fractures[8,15-17] may also be symptoms and signs.

It is critical that no testosterone supplementation should be initiated without a proper and complete evaluation of the patient. This includes a detailed history and full clinical examination, a digital rectal examination (DRE) and serum prostate-specific antigen (PSA) test.[5] The presence of prostate or breast cancer is an absolute contraindication to testosterone therapy. There seems to be no reason for denying a symptomatic, hypogonadal man testosterone therapy on the basis of a theoretical concern of prostate cancer.[18]

Studies on South African subjects

Healthy, ambulant white men aged 20 - 49 years, with normal sperm counts, had mean total testosterone levels in the lower range of normal (Table I).[19] Samples collected from 40 healthy black fathers aged 30 - 39 years, with normal sperm counts, had slightly higher mean total testosterone levels, but still in the lower range (16.9 ± 4.7 nmol/l).[20] It would seem, therefore, that healthy men in South Africa have lower total testosterone values than men in international studies.[13]

TABLE I. TOTAL SERUM TESTOSTERONE CONCENTRATIONS IN MEN WITH NORMAL SPERM COUNTS

Age (years)	Testosterone levels (mean ± SD)*
20 - 29	**14.6 ± 4.9**
30 - 39	**13.9 ± 5.4**
40 - 49	**11.4 ± 5.1**

*Normal range 12.5 - 30.5 nmol/l.

Men with major depressive disorder (MDD)[21,22] were found to have significantly lower total testosterone, bio-available testosterone and free testosterone concentrations than an age-matched control group. Testosterone supplementation should be considered in patients with an incomplete response to antidepressants (Dikobe AM, Van Staden CW, Reif S, Bornman M – unpublished data). South African men with documented coronary artery disease (CAD) showed an inverse relationship between free testosterone levels and the degree of CAD documented on coronary angiography, similar to that reported in international studies.[23-25] Furthermore, 51% of the men had total testosterone levels < 12 nmol/l,[26] which was considerably higher than the 7% reported in healthy males from a similar age group.[9] Low androgen levels are not only associated with adverse cardiovascular risk factors, but may also be a risk factor for development of coronary atherosclerosis.[23]

Testosterone plays an important role in erectile function and up to 40% of ageing men with erectile dysfunction (ED) may have lowered levels of testosterone or other endocrine alterations.[27] In approximately 65% of hypogonadal men, erectile function may improve with testosterone supplementation, and in cases on phosphodiesterase-5 inhibitors, such as sildenafil citrate, with incomplete response, testosterone

may also improve the quality of erection.[28] In men aged 50 - 59 years presenting with ED and with cavernous arterial insufficiency, there is a significantly increased risk of developing coronary heart disease. Screening for cardiovascular risk factors and taking timely preventive action is recommended in men with ED.[29] Men with cavernous arterial insufficiency aged 50 - 59 years are especially prone to developing CAD.

Conclusions

In view of the findings in South African men, obtaining baseline serum testosterone levels in men before the age of 40 years[19] seems mandatory, not only for the future diagnosis and management of LOH, but possibly as an early indicator to screen for CAD, especially in cases with ED. The findings also suggest that urologists should be on the lookout for CAD and cardiologists should screen for LOH in cases with CAD.

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