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Is Testosterone Treatment Good for the Prostate? Study of Safety During Long-Term Treatment

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Conclusions of the study:

The authors concluded that the link between testosterone therapy and developing prostate cancer is a myth. Testosterone replacement therapy is considered safe as far as prostate cancer is concerned, as long as screening and monitoring is part of that protocol. Physicians and patients should understand that a small number of patients could still develop "clinically significant malignancy" even with testosterone treatment.

"The majority of treated men however will have no adverse effect on the prostate but rather many positive benefits on physical and psychological well-being, erectile function, and the factors underlying LUTS. **Physicians and surgeons considering the many potential benefits of [testosterone replacement therapy] for their patients should not be deterred from giving it by theoretical fears, where careful and regular safety monitoring is in place**," they wrote.

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Key points

• The short- and long-term studies of individual, currently-used testosterone preparations have shown that PSA levels do not increase beyond the normal adult range.

• **The present study showed, "no increase in [prostate cancer] rates above that which would be expected in the general population at the same age, and no significant changes in PSA trend above that associated with age."**

Full published report:

Introduction

For some time, there has been concern among physicians that testosterone therapy either leads to prostate cancer or causes undiagnosed prostate cancer to progress. These beliefs have been shown to be a myth; however, many physicians still cite this concern as the main reason for not prescribing testosterone therapy.

The current study aimed to address these concerns and describe the long-term outcomes for 1,365 men who tried different forms of testosterone therapy as part of the UK Androgen Study (UKAS).

Methods

Study participants were self-selected men from the UKAS who had been diagnosed with secondary testosterone deficiency syndrome. Their mean age was 54.2 and 93% were white. The group was treated with testosterone for at least three months and up to 20 years.

The men gave a standardized general medical history and were examined particularly for factors related to low testosterone, such as diabetes, cardiovascular disease, stress, alcohol, medications, loss of libido, erectile dysfunction (ED), and depression for 3-5 years before their first clinic visit. Men were also given digital rectal exams (DREs).

Men visited the clinic at "6 monthly intervals" after symptoms of androgen deficiency were controlled with testosterone therapy. Symptoms and progress of response were assessed using the Andropause Check List and by taking endocrine, biochemical, and hematological profiles.

Men who had primary testosterone deficiency, prostate or breast cancer, "locker room syndrome," "male mid-life crisis," and a primary diagnosis of depression were excluded from participation. Men who had no symptoms and those who wanted physical fitness training were also excluded.

Four types of testosterone preparations were used in the study.

Men were screened for prostate cancer before testosterone therapy began, using urological history, serum PSA readings, and DREs. Men who had abnormal DREs were removed from the study and referred for further testing.

Once testosterone therapy began, PSA levels were measured at 3 months, then every 6 months. DRE was only repeated if a man had lower urinary tract symptoms (LUTS), abnormal PSA readings, concern about increasing PSA levels over time, or a decrease in free/total PSA ratio.

Any man with elevated PSA levels (total PSA > 4.0 ng/mL) had a transrectal ultrasound and a prostate biopsy.

Results

All four testosterone preparation types yielded "highly significant changes in endocrine values between baseline and 1 year." These results were maintained during the treatment period. Among these preparation types, there was no difference in PSA changes or distribution of prostate cancer cases.

1,200 of the 1,365 men had normal PSA throughout their treatment/follow-up period. Twenty-eight were diagnosed with benign prostatic disease. Four men who had normal PSA and DRE results had prostate biopsy because of abnormal results with TRUS or because a patient requested a biopsy as a baseline screening test. Of these four men, one case of prostate cancer was diagnosed.

165 of the 1,365 men had at least one instance of elevated PSA. Fifty-seven of these men had elevated PSA readings at the beginning of the study; of these, four men developed prostate cancer. Nine out of 108 men who developed elevated PSA after having normal readings were later diagnosed with prostate cancer.

Of 34 men who had prostate biopsy for elevated PSA, 13 men had prostate cancer and 21 had negative biopsy.

Assessment of Prostate Cancer Cases

Fourteen men between the ages of 57 and 78 were diagnosed with prostate cancer after one to twelve years of testosterone treatment. Most of these men had had a rise in PSA before diagnosis. All of these cases were clinically localized. Most of the men diagnosed with prostate cancer had used more than one type of testosterone treatment. However, the risk of developing prostate cancer was not considered statistically significant among different preparations. Two of the fourteen cases of prostate cancer were considered high risk. The remaining twelve men were classified as clinical stage T1c. All cases of prostate cancer were "suitable for treatment with curative intent."

The authors note that each type of testosterone preparation increased free PSA in proportion to total PSA. The free/total ratio stayed constant or increased with treatment. This is "a further indication of the intrinsic safety of all forms of [testosterone replacement therapy]." In this study, some reduction in this ratio was observed in those cases that developed prostate cancer, changing from 0.23 to 0.17 between presentation and the time of diagnosis. Half the cases had low mean ratios (<0.10) for up to 3 years before the clinical diagnosis was made, supporting the suggestion that a low free PSA ratio may be actually be predictive for prostate cancer

Discussion

The authors acknowledged several limitations to this study. For example, biopsy protocols of the time were used and may not be the same at this time. Also, some patients were lost to follow-up. Taking limitations into consideration, however, the authors concluded that testosterone therapy is safe for men with testosterone deficiency syndrome as long as therapy

is accompanied by careful monitoring. Both physicians and patients should understand any risks associated with testosterone therapy and prostate cancer.

The authors also noted that their approach for diagnosing prostate cancer was less aggressive than that taken in past prostate cancer screening studies. A more aggressive approach might have yielded more cases of prostate cancer. However, the authors stated, "Intensive screening, particularly in an aging population, inevitably carries a substantial risk of detecting either clinically insignificant cancer, defined as disease that would not threaten the quality or duration of the individual's life."

Evidence for the safety of testosterone therapy was further discussed:

• Past studies, including one from the Journal of Sexual Medicine published last year, confirm that testosterone therapy is safe for the prostate and does not increase the risk of either prostate cancer or prostatic hyperplasia.

• In men with missing or malfunctioning testes who are treated with life-long testosterone therapy, PSA levels are in line with those of the normal population and prostate cancer is "very rarely reported."

• In the UK's "Yellow Card – Adverse Reactions Reporting System," only three deaths were reported out of 185 patients. Only two of those deaths may have been related to prostate cancer.

• The short- and long-term studies of individual, currently-used testosterone preparations have shown that PSA levels do not increase beyond the normal adult range.

• The present study showed, "no increase in [prostate cancer] rates above that which would be expected in the general population at the same age, and no significant changes in PSA trend above that associated with age."

The authors also suggested that testosterone therapy may benefit men with ED and LUTS.

Conclusions

The authors concluded that the link between testosterone therapy and developing prostate cancer is a myth. Testosterone replacement therapy is considered safe as far as prostate

cancer is concerned, as long as screening and monitoring is part of that protocol. Physicians and patients should understand that a small number of patients could still develop "clinically significant malignancy" even with testosterone treatment.

"The majority of treated men however will have no adverse effect on the prostate but rather many positive benefits on physical and psychological well-being, erectile function, and the factors underlying LUTS. Physicians and surgeons considering the many potential benefits of [testosterone replacement therapy] for their patients should not be deterred from giving it by theoretical fears, where careful and regular safety monitoring is in place," they wrote.

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