Testosterone therapy in hypogonadal men and potential prostate cancer risk: a systematic review
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CRD summary
The authors concluded that there was no evidence that testosterone treatment in men with hypogonadism increased the risk of prostate cancer. The authors’ conclusions appeared to reflect review findings, but the lack of reporting of review methods and study quality and reliance upon generally small short-term studies meant that they may not be robust.

Authors’ objectives
To determine if testosterone therapy for hypogonadism in men increases the risk of prostate cancer.

Searching
MEDLINE and EMBASE were searched from 1970 through 2008 for studies published in English. Search terms were reported. References in journal articles, conference proceedings and books were screened and study investigators contacted for further references.

Study selection
Studies of any design that evaluated the effects of monotherapy with testosterone therapy for signs and symptoms of hypogonadism or an abnormally low or low-normal testosterone level of any aetiology in adult men were eligible for inclusion. Studies had to assess prostate cancer confirmed histologically. Studies could be in men with or without a history of prostate cancer.

The included studies evaluated different formulations, modes of administration and doses of testosterone (details were reported). The age of patients ranged from 18 to 86 years. Outcomes reported were the incidence of prostate cancer during testosterone therapy, changes in levels of prostate-specific antigen and Gleason grade of cancer. The duration of follow up ranged from two months to 10 years.

The authors stated neither how papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
For each study, numbers of patients with outcomes of interest were presented.

The authors stated neither how data were extracted for the review nor how many reviewers performed the data extraction.

Methods of synthesis
The studies were grouped by study design and the presence or absence of a history of prostate cancer and combined in a narrative synthesis.

Results of the review
Forty-four studies were included.

Men without a history of prostate cancer were assessed in 11 placebo-controlled RCTs (n=893) and 29 non-placebo controlled studies (n=1,732, which comprised: one case series n=20; 15 prospective studies n=1,354; five retrospective studies n=349; and eight case reports n=9).

Men with a history of prostate cancer were assessed in four studies: one prospective (n=5) and three retrospective case
Men without a history of prostate cancer:

Randomised-placebo controlled trials (11 studies, nine with follow up of one year or less): rates of prostate cancer were similar for testosterone and placebo–treated groups (1.3% versus 1.5%; overall seven out of 542 testosterone-treated men developed prostate cancer). The incidence across studies ranged from 0% in both groups to 9.5% in a testosterone-group versus 21% for a placebo group in one study; this study was the only one that routinely performed end-of-study prostate biopsies.

Non-placebo controlled studies (21 studies): seven studies reported a total of 12 cases of prostate cancer; the incidence per study ranged from 1.2% to 4.5%. One retrospective study examined 20 cases of prostate cancer in men who received testosterone; 11 cancers were detected in the first two years of testosterone therapy and nine were detected 28 months to eight years after the start of treatment.

Men with a history of prostate cancer:

The four studies (n=53) found no evidence of a recurrence of prostate cancer over follow up that ranged from 0.5 to 12 years. Following treatment, prostate-specific antigen levels were less than 1ng/mL after 8.5 years in one retrospective study and undetectable for up to 12 years in two other retrospective studies.

Authors' conclusions

There was no evidence that testosterone treatment in men with hypogonadism increased the risk of prostate cancer.

CRD commentary

The review question was clearly stated. Inclusion criteria were defined for intervention, participants and outcomes; criteria for study design were broad. Only two relevant sources were searched. No attempts were made to minimise language bias and it was unclear whether attempts were made to minimise publication bias. Methods used to select studies and extract data were not described, so it was unknown whether efforts were made to reduce reviewer errors and bias. A narrative synthesis was appropriate. In placebo-controlled trials, the overall cancer rate in each group was reported and prostate-specific antigen results were reported as changes from baseline in each treatment group, rather than as differences between treatment groups; this plus a lack of clarity in the number of cancer cases made it difficult to interpret the results. The authors acknowledged some limitations of the evidence, such as short-term follow up. In addition, evidence about men with previous prostate cancer was based on only 53 men. Small short-term studies provide only limited evidence. The authors' conclusions appeared to reflect review findings, but the lack of reporting of review methods and study quality and reliance upon generally small short-term studies meant that they may not be robust.

Implications of the review for practice and research

Practice: The authors stated that before starting testosterone treatment in men with hypogonadism, a prostate biopsy should be performed in men with higher prostate-specific antigen levels. Patients who receive testosterone therapy should be closely and regularly monitored and should be referred if prostate-specific antigen levels increased or an abnormality was found on digital rectal examination.

Research: The authors did not state any implications for future research.

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Bibliographic details


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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.