0022-5347/02/1686-2431/0
THE JOURNAL OF UROLOGY®
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Vol. 168, 2431–2433, December 2002
Printed in U.S.A.
DOI: 10.1097/01.ju.0000032178.16280.e0

SERUM TRIIODOTHYRONINE IS INCREASED IN MEN WITH PROSTATE CANCER AND BENIGN PROSTATIC HYPERPLASIA

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ABSTRACT

Triiodothyronine is the active thyroid hormone produced by de-iodination of the precursor thyroxine that is necessary for the growth of prostate cancer cells in vitro. For this reason we assessed serum triiodothyronine levels in men with localized prostate cancer, benign prostatic hyperplasia (BPH) and controls in the same age group.

Materials and Methods: We studied 161 men referred for treatment of localized prostate cancer, 20 with BPH and 27 controls. Serum triiodothyronine was determined by fluorometric immunoassay and a commercially available instrument.

Results: Men with BPH had the highest triiodothyronine levels, followed by those with prostate cancer. Controls had the lowest triiodothyronine. There was significant triiodothyronine variation among the 3 groups (1-way ANOVA $p = 0.001$). In men with BPH serum triiodothyronine was significantly different from that in men with prostate cancer (Tukey's multiple range test $p = 0.013$). Men with prostate cancer had serum triiodothyronine that was significantly different than in controls ($p = 0.048$), as did those with BPH ($p < 0.001$). Because serum triiodothyronine normally decreases with age, we performed multivariate analysis of variance controlling for age. There was a significant decrease in serum triiodothyronine with age ($p = 0.020$). There was also significant triiodothyronine variation among the 3 subject groups independent of age ($p < 0.001$).

Conclusions: Urologists are actively seeking additional biomarkers of prostate cancer aggressiveness. Many prostate cancers are quite indolent and may never cause a problem but it is impossible to identify such tumors with certainty. With more and better biomarkers many older men with prostate cancer may be spared the rigors of radiation therapy and/or surgery as well as complications. Triiodothyronine may be such a biomarker. Also, new prostate cancer and BPH therapies may be directed toward inhibiting the mitogenic effects of triiodothyronine.

KEY WORDS: prostate; prostatic neoplasms; prostatic hyperplasia; tumor markers, biological; triiodothyronine

Triiodothyronine is the active thyroid hormone produced by de-iodination of the precursor thyroxine. Triiodothyronine is necessary for the growth of prostate cancer cells in vitro. For example, a special serum-free defined medium that can support short-term, long-term and clonal growth of the human prostatic carcinoma cell lines LNCaP, DU 145, PC-3 and ALVA-31 must contain triiodothyronine.[1] Because triiodothyronine also has an important role in the regulation of prostate cell growth and differentiation,[2] we compared serum triiodothyronine in men with localized prostate cancer, benign prostatic hyperplasia (BPH) and controls in the same age group. We hypothesized that if increased triiodothyronine were detected levels in men with prostate cancer, triiodothyronine may be used as a marker for this disease.

MATERIALS AND METHODS

Study participants were identified at urology, radiation oncology and other clinics. The study accrual period was 3.5 years (1999 to 2002). All eligible patients were asked to participate. Eligibility criteria were an initial diagnosis of prostate cancer based on increasing prostate specific antigen or abnormal physical examination that was confirmed histologically. All participants provided informed consent and the study had Institutional Review Board approval. All patients

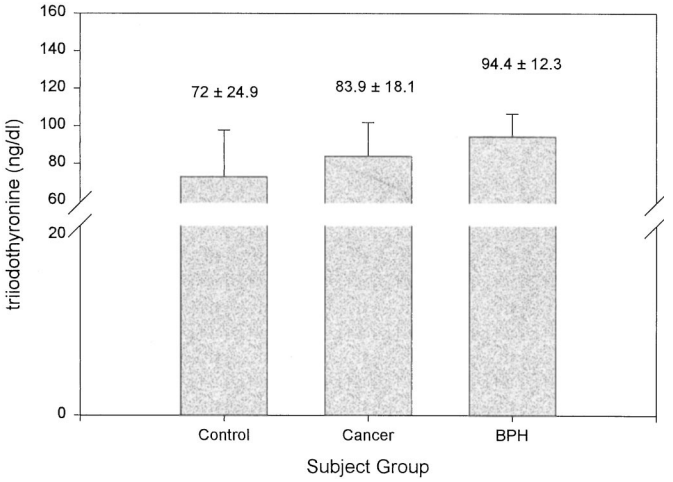

FIG. 1. Mean serum triiodothyronine in men with prostate cancer, BPH and controls differed significantly ($p = 0.001$). Serum triiodothyronine was significantly different in men with BPH versus prostate cancer (Tukey's multiple range test $p = 0.013$), prostate cancer versus controls ($p = 0.048$) and BPH versus controls ($p < 0.001$).

Accepted for publication July 5, 2002.

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† Financial interest and/or other relationship with Amgen, Mid Atlantic Thermotherapy and Pro Seed.

‡ Financial interest and/or other relationship with Ilex Oncology, Kendle, NERI Research Institute and PhotoCure ASA.

§Financial interest and/or other relationship with Bard Urologic.

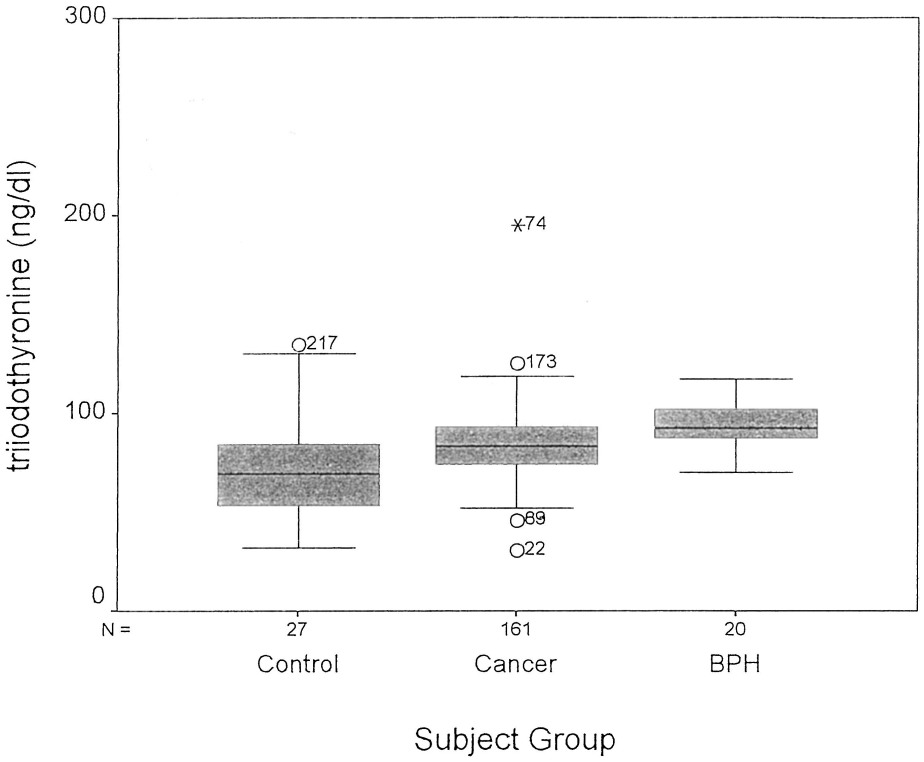

FIG. 2. Serum triiodothyronine in men with prostate cancer, BPH and controls. Values on x axis indicate number of cases per group. Boxes represent 25th to 75th percentiles. Horizontal line within boxes represents median (50th percentile). Whiskers indicate smallest and largest values per group that were not outliers (*o*, case number), that is cases between 1.5 and 3 box lengths from box boundaries. Asterisk indicates that case 74 in cancer group represented extreme value more than 3 box lengths from box boundaries.

with BPH were being treatment for this condition and the diagnosis had been confirmed by at least 1 needle biopsy of the prostate. Controls had no history of cancer, thyroid disease or treatment for BPH. They were age matched to patients in the BPH and cancer groups. We studied 161 men referred for the treatment of localized prostate cancer, 20 with BPH and 27 controls. Serum triiodothyronine was determined with a fluorometric immunoassay and a commercially available instrument.

RESULTS

Mean age of study participants plus or minus SD was 68 ± 8.5 years (range 46 to 96), including 67 ± 7.9 in those with prostate cancer, 74 ± 6 in those with BPH and 73 ± 10 in controls. Men with BPH had the highest triiodothyronine, followed by those with prostate cancer, while controls had the lowest triiodothyronine (normal at our laboratory 45 to 137 ng./dl.). There was significant triiodothyronine variation among the 3 groups (1-way ANOVA $p = 0.001$, figs. 1 and 2). In men with BPH serum triiodothyronine was significantly different than in men with prostate cancer (Tukey's multiple range test $p = 0.013$). Patients with prostate cancer had significantly different serum triiodothyronine than controls ($p = 0.048$), as did those with BPH ($p < 0.001$).

Because serum triiodothyronine normally decreases with age,[3,4] we performed multivariate analysis of variance controlling for age. There was a significant decrease in serum triiodothyronine with age ($p = 0.020$). There was also significant triiodothyronine variation among the 3 subject groups independent of age ($p < 0.001$).

DISCUSSION

Epidemiological studies have identified no definite relationship among triiodothyronine, thyroid disease, BPH and prostate cancer. A study of localized and metastatic prostate cancer revealed no abnormality in triiodothyronine.[5] In another series there was a marginally decreased incidence of prostate cancer in men with myxedema.[6] Nevertheless, our finding of an association of serum triiodothyronine with BPH and prostate cancer is not surprising due to the mitogenic potential of triiodothyronine. It supports our stated hypothesis that triiodothyronine may be useful as a marker for prostate cancer. Moreover, we have previously reported an association of elevated serum triiodothyronine with the increased risk of recurrent prostate cancer.[7]

Urologists are actively seeking additional biomarkers of prostate cancer aggressiveness. Many prostate cancers are quite indolent and may never cause a problem but it is impossible to identify such tumors with certainty. Therefore, further studies of serum triiodothyronine level in patients with prostate cancer may be worthwhile. Also, a study directly correlating triiodothyronine with the outcome of prostate cancer should be done.

CONCLUSIONS

With more and better biomarkers many older men with prostate cancer may be spared the rigors of radiation therapy and/or surgery as well as complications. Also, new prostate cancer and BPH therapies may be directed toward inhibiting the mitogenic effects of triiodothyronine.

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