461

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MESSENGER RNA LEVELS AND ENZYME ACTIVITIES OF 5 ALPHA-REDUCTASE TYPE 1 AND 2 IN THE HUMAN BENIGN PROSTATIC HYPERPLASIA (BPH) TISSUES

Aims of Study

Benign prostatic hyperplasia (BPH) is the most common proliferative disease affecting men and causes obstructive uropathy. BPH development requires testicular androgens and aging. The principle prostatic androgen is dihydrotestosterone (DHT).Testosterone is converted to DHT by the enzyme 5alpha-reductase. Two distinct 5alpha-reductase enzymes, types 1 and 2, have been identified. 5alpha-reductase type1 is the predominant enzyme in extraprostatic tissues, and 5alpha-reductase type 2 predominates in the prostate. Studies on the prostatic localization of the two isoenzymes have yielded contradictory results. While some authors have reported the presence of only 5 alpha-reductase type 2 in the human prostate, a few reports have suggested that both types of 5 alpha-reductase can be detected in this tissue. Finasteride has been used for the treatment of BPH and its major effect is through suppression of 5 alpha-reductase type 2, because it has a much lower affinity for the type 1 isoenzyme. Several studies have demonstrated that drugs that inhibit both type 1 and 2 isoenzymes have showed increased efficacy in the treatment of BPH. These studies suggested that 5 alpha-reductase type 1 may play a role in maintaining prostate enlargement. The purpose of this study is to characterize the possible role of 5 alpha-reductase Type 1 in BPH tissues.

Methods

Prostatic tissues were obtained from 15 patients who were underwent total cystectomy because of bladder cancer. All prostatic tissues were diagnosed BPH by reviewing histological sections. Localizations of both type 1 and 2 isoenzymes in prostate were examined by immnunohistochemical staining. Expressions of the both isoenzymes mRNA in prostate were quantified and compared by a real-time quantitative RT-PCR with TaqMan system. Both type 1 and 2 isoenzymes mRNA levels were finally determined as the copy number per microgram of total RNA extracted from each tissue sample. Copy numbers for standard curves of both isoenzymes were calculated using the mean molecular weight of recombinant RNA of type 1 and 2 isoenzymes. 5alpha-reductase assay was performed, type 1 at pH 7.0 and type 2 at pH 5.5.

Results

Immnunohistochemical localization study showed that type 1 isoenzyme was expressed predominantly in epithelial cells of prostate, whereas type 2 isoenzymes was expressed in both stromal and epithelial cells of prostate. The real time quantitative RT-PCR assay demonstrated that while 321-1387 $X10^5$ copy numbers of 5 alpha-reductase type 1 mRNA were detected in 1 microgram of total RNA isolated from prostate tissues, 99-678 $X10^5$ copy numbers of 5 alpha-reductase type 2 mRNA were detected. 5 alpha-reductase activities were present in all prostate tissues, at pH 7.0 and 5.5. There were significant associations between enzyme activity at pH 7.0 and type 1 isoenzyme mRNA expression and between the activity at pH 5.5 and type 2 mRNA expressions.

Conclusions

In conclusion, we demonstrated that 5alpha-reductase type I had a certain enzyme activity in prostate and this result supported the hypothesis that 5 alpha-reductase type 1 may play a significant role in maintaining prostate enlargement as well as 5 alpha-reductase type 2.