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MODERN APPROACH TO THE TREATMENT OF BENIGN PROSTATIC HYPERPLASIA.

Annotation

Current treatments for BPH include watchful waiting, drug therapy, and surgery. 6 Most patients receive drug therapy, mainly including α- blockers and 5-α-reductase inhibitors (5-ARIs), when LUTS first occur. 7 However, only 5-ARIs are effective in reducing prostate size by approximately 20-30% in 4-6 months. , which has a higher affinity for androgen receptors (AR). Decreased DHT concentrations in the prostate cause apoptosis and necrosis of AR-dependent cells and ultimately reduce prostate size 8, 9. Finasteride and dutasteride are the two main 5-ARV drugs that target different isotypes of 5-AR. Finasteride specifically inhibits SRD5A2, which is mainly expressed in the prostate.

Keywords: *5-alpha reductase, SRD5A2 , adrenergic blockers , prostate, inhibitor,*

Benign prostatic hyperplasia (BPH) is histologically characterized by aberrant proliferation of epithelial and stromal cells in the transition zone of the prostate 1. The incidence of BPH increases with age; Approximately 50% of men aged 50 years and more than 80% of men aged 80 years have pathological manifestations of BPH 2, 3. The pattern of prostate growth indicates that approximately 25% of men will develop clinical symptoms of BPH during their lifetime 4 BPH impairs the quality of life of older men due to lower urinary tract symptoms (LUTS), including urination and urinary retention 1, 5.

Previous studies have reported significant variability in SRD5A2 protein expression in BPH samples, and 10–36.5% of BPH samples did not express SRD5A2 protein.

Materials and methods

Immunohistochemistry (IHC) was performed as previously described by Lin et al . 9. Briefly, sample sections were incubated with anti-SRD5A2 antibody (Novus Biological Inc. , Centennial , CO, USA, NBP1-46510) according to the manufacturer's recommendations at a concentration of 1:1500. Negative controls were used throughout the immunostaining protocol . Three representative areas from each sample were randomly selected under 40× magnification for assessment of immunoreactivity by two genitourinary pathologists. One hundred cells randomly selected from the epithelium were manually counted in each representative section. Each cell was scored on a scale from 0 to 3 according to the intensity of staining. A visual score was then created for each sample ranging from 0 to 300. A score of 0 to 100 was defined as weak expression and a score of 101 to 300 as strong expression.

Results

The expression of SRD5A2 varies in different BPH tissues and cells. A total of 59 BPH samples were collected to evaluate SRD5A2 expression in different prostate tissues. Immunohistochemical staining showed that SRD5A2 was expressed mainly in prostate transition zone epithelial cells, and a small amount of SRD5A2 was expressed in stromal cells, which is consistent with previous studies 6, 7, 18. In our study, SRD5A2 expression varied among patients. Eight cases (13.6%) of BPH showed negative expression of SRD5A2, 17 cases (28.8%) showed weak expression and 34 cases (57.6%) showed strong positive expression. Expression of SRD5A2 in BPH-1 and RWPE-1, two classical prostate epithelial cell lines, was detected by Western blotting.

had no differences in BPH tissues with different expression of SRD5A2.

To test whether miR-1199-5p could regulate SRD5A2 expression, we transfected miR-1199-5p mimics into RWPE-1 cells, which strongly expressed

SRD5A2, and miR-1199-5p inhibitors into BPH-1 cells, which weakly expressed SRD5A2 . qRT -PCR and Western blotting were used to detect changes in SRD5A2 mRNA levels and protein expression, respectively, after transfection. We found that SRD5A2 mRNA (Figure 3A) and protein expression (Figure 3B) were significantly decreased after transfection of RWPE-1 cells with miR-1199-5p mimics. While the protein expression of SRD5A2 was significantly increased in BPH-1 cells after transfection with miR-1199-5p inhibitor. Transient transfection of miR-1199-5p mimics and wild-type SRD5A2 3′UTR reporters into 293T cells revealed a significant decrease in luminescence, which was not observed in the mutant version of the reporter (Fig. 3E). These results confirmed that miR-1199-5p could bind to the 3′UTR of SRD5A2 and inhibit its expression.

Finasteride was also found to have an effect on the viability of BPH-1 and RWPE-1 after transfection with miR-1199-5p mimics and inhibitors using flow cytometry . As we previously reported, finasteride did not induce BPH-1 apoptosis, as demonstrated by decreased expression of SRD5A29. However, increasing SRD5A2 expression in BPH-1 cells through transfection of the miR-1199-5p inhibitor did not result in the development of finasteride . (100 μM) sensitivity in BPH-1 cells (Fig. 3F). Notably, finasteride (100 μM) promoted RWPE-1 apoptosis and suppressed SRD5A2 expression through miR-1199-5p transfection, mimicking inhibition of apoptosis progression (Figure 3G). Various expressions of AR may explain this phenomenon. In particular, RWPE-1 cells express AR, whereas BPH-1 cells lack AR 22, 23. Thus, these data indicate that miR-1199-5p may downregulate SRD5A2 expression and influence prostate cell apoptosis.

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