

HIGHER EXPRESSION OF PHOSPHODIESTERASE-5 IN THE ANTERIOR FIBROMUSCULAR STROMA OF THE HUMAN PROSTATE

Hypothesis / aims of study

Phosphodiesterase type 5 (PDE5) inhibitors have been proven as effective pharmacotherapy for men suffering from erectile dysfunction and also for men suffering from lower urinary tract symptoms (LUTS). Although distribution pattern of PDE5 in human prostate was analysed in several studies, the experimental data concerning the expression location and level of PDE-5 expression in the prostate have had considerable inter-experimental variations [1]. Thus, more detailed analysis of PDE5 expression location according to the zonal anatomy of the prostate could enhance understanding of the effective targeting tissue of PDE5 inhibitors.

Interestingly, possible functional contribution of the anterior fibromuscular stroma (AFMS) of the human prostate to the urinary function has been reported [2, 3]. The peculiar innervations pattern was seen in the AFMS compared with the other glandular zone [2]. These suggested possible function specific to AFMS different from glandular zones. The objective of this study is to compare the expression of PDE5 in the AFMS with that in the other glandular zone or the bladder neck using immunohistochemistry with computer-assisted image-analysis technique.

Study design, materials and methods

Total 18 human prostate and bladder specimens were obtained from cystoprostatectomy for bladder cancer and radical prostatectomy for prostate cancer. The paraffin serial sections were used for H&E stain and the immunohistochemistry for PDE5 antibody. Selected fields were analysed from the AFMS, stromal hyperplasia in the transition zone (TZ stroma), glandular hyperplasia in the transition zone (TZ gland), the peripheral zone (PZ), and the bladder neck in order to quantify. The ratio of immunoreactive smooth muscle area of PDE5 to the area of smooth muscle in H&E stain was calculated using computer-assisted image analysis system.

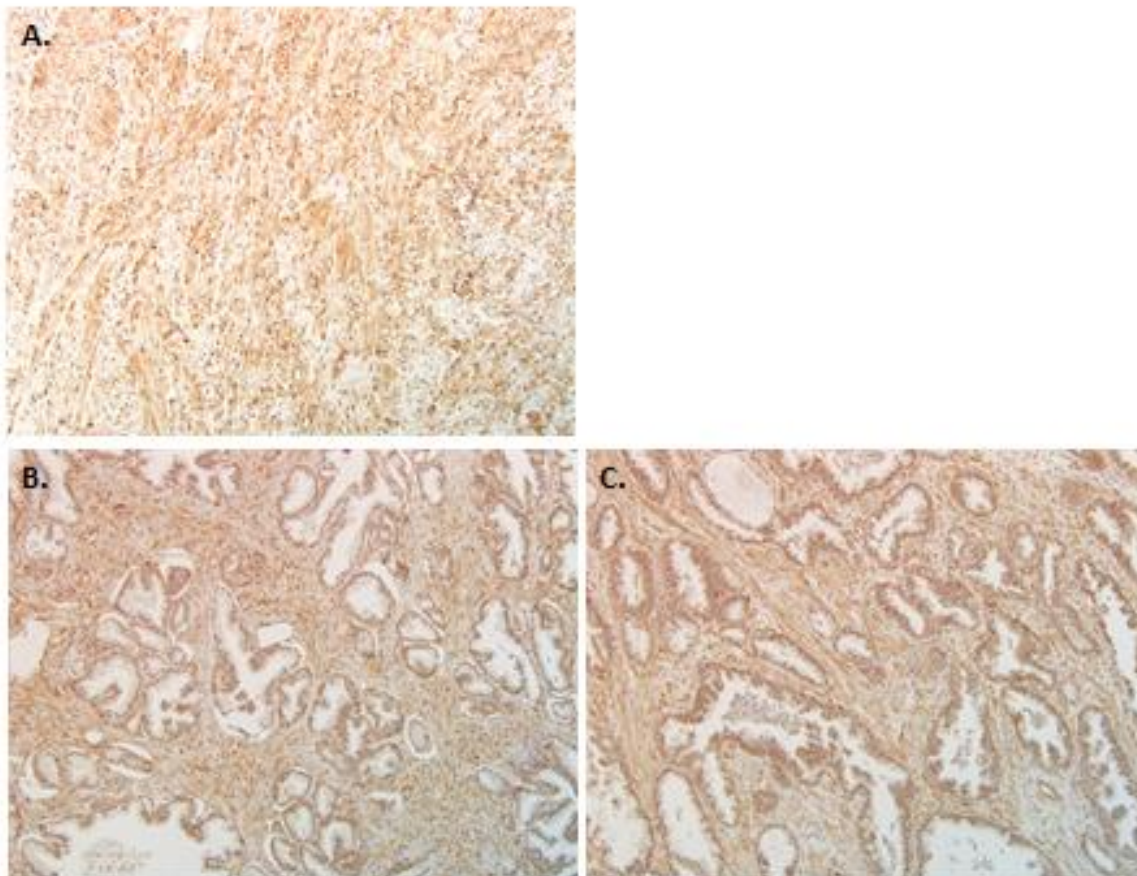


Figure.1

Immunohistochemistry in the AFMS (A), the glandular hyperplasia of the transition zone (B) and the peripheral zone (C). AFMS shows abundant immunoreactive smooth muscle bundles. TZ and PZ show relatively scanty PDE5 immunoreactivity in the stroma. (magnification 100X)

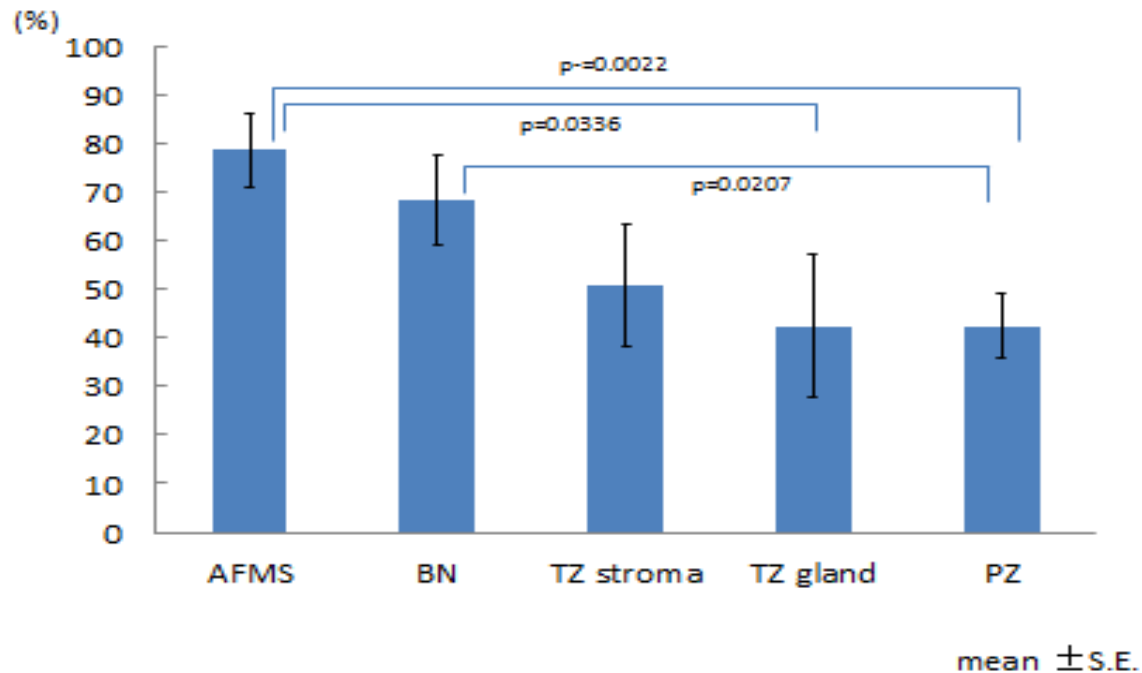


Figure. 2
The ratio of PDE5 immunoreactive area to smooth muscle area calculated by computer-assisted image analysis

Results

Image analysis showed that the average ratio of immunoreactive area of PDE5 to the area of smooth muscle in H&E stain was 78.5% in the AFMS, 68.2% in the bladder neck, 50.8% in the TZ stroma, 42.3% in the TZ gland and 42.4% in the PZ, respectively. There was the significantly higher expression of PDE5 in the AFMS than in the TZ gland ($p=0.0336$) or PZ ($p=0.0022$). There was no significant difference of PDE5 expression between the AFMS and the bladder neck or TZ stroma.

Interpretation of results

The higher expression of PDE 5 was identified in the AFMS than in the TZ gland or PZ. The results of this study showed the zonal difference of PDE5 expression suggesting that the AFMS could be the main prostatic target tissue of PDE5 inhibitors in pharmacotherapy for LUTS. Further assessment of possible specific function of AFMS was warranted.

Concluding message

This study showed the higher expression of PDE5 in the AFMS than in other glandular zone of the prostate. AFMS could be the main target tissue of PDE5 inhibitors in the human prostate.

References

1. Urology. 2013;81(3):480-486
2. The Prostate. 2001;48(4):242-7.
3. Ultrasound in medicine & biology. 2004;30(5):575-81

Disclosures

Funding: None **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** Kyoto Prefectural University of Medicine **Helsinki:** Yes **Informed Consent:** Yes