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QUANTITATION OF ALPHA 1 A- AND ALPHA 1 D-ADRENOCEPTOR MESSANGER RNA IN BENIGN PROSTATIC HYPERPLASIA TISSUES USING REAL-TIME PCR

Aims of Study

To treat symptomatic benign prostatic hyperplasia (BPH) alpha 1-adrenoceptor (AR) antagonists with little antagonism at alpha 1b-AR have been chosen to avoid orthostatic hypotension. In BPH tissues alpha 1a-AR are thought to predominate, but either alpha 1a or alpha 1d-AR antagonists can alleviate BPH symptoms according to Japanese experience. We therefore hypothesized that prostatic expression of alpha 1a- and alpha 1d -AR varies quantitatively between patients with symptomatic BPH.

Methods

Prostatic tissue specimens were obtained from nine patients undergoing radical cystectomy to treat invasive bladder cancer at our institution or at affiliated hospitals. All were confirmed to have symptomatic BPH as well, according to International Prostate Symptom Scores (I-PSS >17) and uroflowmetry (maximum flow rate <10 ml/sec). Patients had no treatment with alpha 1a -AR antagonists for at least 1 month prior to the operation. Specimens were taken from the central area and the peripheral (subcapsular) area. All prostatic tissues were diagnosed BPH by reviewing histological sections. Localizations of both alpha 1a - and alpha 1d -AR receptors in prostate were examined by immnunohistochemical staining. and mRNA expressions for these subtypes were quantitated by real-time quantitative reverse transcription-polymerase chain reaction.

Results

The immunohistochemistry showed that the alpha 1a-AR subtype was localized in the stromal component, and was not detected in epithelial cells. Similarly alpha 1d-AR was detected only in stromal cells, predominantly smooth muscle cells, and not in epithelial cells. In central and in peripheral areas of the prostate respectively, 3.76 to $37.2x10^7$ and 5.4 to $68.1x10^7$ copies number of alpha 1a-AR mRNA per microgram of total RNA were detected. Copy numbers of alpha 1d-AR mRNA were 0.46 to $29.2x10^7$ in the central area and 0.64 to $58x10^7$ in the peripheral area. No statistically significant difference in the amount of alpha 1a- or alpha 1d-AR mRNA was noted between central area and peripheral areas. The amount of alpha 1a-AR mRNA was consistently higher than that of alpha 1d-AR mRNA regardless of location in the prostate. However, ratios of alpha 1a- to alpha 1d-AR mRNA expression were distributed in a wide range in both areas (1.0 to 8.4).

Conclusions

Our data indicated that ratios of alpha 1a- to alpha 1d-AR expressions differ between patients. Some patients can be treated successfully with alpha 1-AR antagonists specific for alpha 1a-AR, but others may have better results using antagonists with at least some activity at alpha 1d-AR.An ideal therapeutic antagonist for treating BPH symptoms should block both alpha 1a- and alpha 1d-AR.