**558**

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# INCREASED PROSTATE SMOOTH MUSCLE CONTRACTIONS AND REDUCED RELAXATIONS IN MIDDLE-AGED RATS.

Hypothesis / aims of study

The increase in elderly population is becoming a worldwide phenomenon. Clinical studies suggest a strong relationship between aging and genitourinary tract diseases, being the benign prostatic hyperplasia (BPH) the most prevalent disease in men [1]. Besides prostate enlargement, BPH is characterized by increased smooth muscle tone, thus contributing to overactive bladder and lower urinary tract symptoms (LUTS). $\alpha$-adrenoceptors are highly expressed in prostate of various animal species. ATP, via purinergic P2X1 receptors, also contributes to the contractile response, and is considered a co-transmitter with noradrenaline in prostate. Other neurotransmitters and signalling regulate the tone of prostatic smooth muscle including Rho-kinase, nitric oxide-cGMP and β-adrenoceptor-cAMP pathways. Previous studies showed aging-dependent reduction of prostate nitrergic innervation and distribution of autonomic receptors [2,3]. The aim of the present study was to evaluate the influence of aging in the prostatic smooth muscle (PSM) reactivity in middle-aged rats, looking at both the relaxant and contractile machinery.

Study design, materials and methods

Wistar rats were divided into two groups: (a) young (14-15 weeks) and (b) middle-aged rats (37-38 weeks). Concentration-response curves to the contractile agents phenylephrine (α1-adrenoceptor agonist) and α,β-methylene ATP (purinergic P2X1 agonist), as well as to the relaxing agents isoproterenol (non-selective β-adrenoceptor agonist), sodium nitroprusside (SNP; nitric oxide donor) and Y27632 (Rho kinase inhibitor) were obtained in PSM. Neurogenic contractions produced by electrical-field stimulation (EFS; 1-32 Hz, 50V, 10 sec) were also performed. The levels of cAMP in prostate homogenate were determined by ELISA assays.

Results

A significant increase in phenylephrine- and α,β-methylene ATP-induced PSM contractions were observed in middle-aged rats (4.60±0.33 and 2.69±0.13 mN, respectively; $P<0.05$) compared with young rats (3.52±0.15 and 2.03±0.2 mN, respectively). EFS-induced PSM contractions were also higher in middle-aged group (32 Hz: 3.98±0.39 mN, $P<0.05$) compared with control group (2.52±0.25 mN). In contrast, the PSM-induced relaxations in response to SNP, isoproterenol and Y27632 were lower in middle-aged rats (59.4±4%, 48.6±4% and 76.1±3%, respectively; $P<0.05$) in comparison with young rats (76.37±1%, 63.5±3% and 92.3±4%, respectively). The cAMP levels in prostate homogenate were 25% lower ($P<0.05$) in middle-aged compared with control group.

Interpretation of results

Our findings show that PSM from middle-aged rats exhibit hypercontractility in response to α1-adrenergic and purinergic P2X1 receptor activation, which is associated with impaired cAMP- and cGMP-mediated relaxations. Whether such alterations contribute to BPH development is under current investigation.

Concluding message

Prostatic changes in middle age can contribute to the development of LUTS secondary to BPH in elderly. The identification of pathways involved in the development of BPH could help to clarify the pathophysiology of the disease, as well as to provide new therapeutic targets for this disease treatment.

References

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