CONCLUSIONS AND DISCUSSION

The stiffness dose response curves obtained using the PZT biosensor method were similar to those using the conventional tissue bath isometric techniques(1). While contractility has been measured under *in vitro* conditions using tissue strips which are stretched and suspended in a bathing solution, there has not been to date an equally feasible approach which allows for the determination of un-stretched bladder stiffness. Using this method it is concluded that ovariectomy significantly increases bladder stiffness in response to low doses of cholinergic stimulation in comparison to the estrogen supplemented rats. The results obtained from this study using the PZT transducer demonstrate the potential of Estrogen manipulation in modulating the mechanical charactristics of the bladder. We project that by using this alternative method of assesing the effect of pharmacologic stimulation on the bladder the influence of hormones on the bladder as well as the prostate can be objectively evaluated. Finally we expect that this approach, which uses smaller amounts tissue than isometric recordings may prove appropriate in the evaluation of tissue segments obtained from biopshies.

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Title (*type in CAPITAL LETTERS, leave one blank line before the text*):

UROTHELIUM MODULATES DETRUSOR SMOOTH MUSCLE CONTRACTILITY IN THE RABBIT

Aims of Study: Studies have demonstrated that the urothelium may play an inhibitory role in modulating detrusor smooth muscle contractility. We studied possible mechanisms involved in urothelial regulation of detrusor smooth muscle tone.

Methods: One half of each bladder obtained from 15 male New Zealand white rabbits were de-mucosalized. Longitudinal strips of each bladder body were weighed and processed for isometric tension measurement. In strips with urothelium (Uro+) and without urothelium (Uro-), the reactivity to electrical field stimulation (EFS), carbachol, methoxamine and isoproteronol were studied at baseline tension. The reactivity to EFS and carbachol was then re-examined following tissue treatment with atropine, guanethidine, indomethacin and nordihydroguaiaretic acid (NDGA), a lipoxygenase inhibitor.

Results: Removal of the urothelium altered spontaneous contractility of the bladder strips. At baseline, Uro- strips demonstrated significant increases in the frequency, amplitude and duration of spontaneous contractions and in contractile response to EFS, carbachol and methoxamine relative to Uro+ strips. The contractile response of Uro- strips to EFS and carbachol were not significantly altered in the sole presence of indomethacin. However, they were significantly reduced in the presence of NDGA, and more so with NDGA + indomethacin. In the presence of atropine, both Uro+

and Uro- strips demonstrated a similar decrease in contractile response to EFS and carbachol. Guanethidine failed to normalize the differences in the contractility of Uro- and Uro+ bladder strips. Relaxation responses to the beta adrenergic agonist isoproteronol were significantly reduced in the Uro- strips.

Conclusions: Removal of the urothelium resulted in significant increases in baseline contractile instability and the contractile response of isolated rabbit bladder strips to EFS, carbachol, and methoxamine, while impairing the relaxatory response to isoproteronol. These observations confirm the inhibitory effect of the urothelium on bladder tone. The significant reduction of hypercontractility in Uro- strips in the presence of NDGA suggests a regulatory role for leukotrienes. These agents are known to directly cause smooth muscle contraction. In Uro- tissues, the observed loss of detrusor inhibition normally induced by isoproterenol suggests an important role for the bladder urothelium in adrenergic control over bladder contractility. Urothelial injury may thus be an important mechanism in the development of detrusor instability and other conditions characterized by detrusor overactivity.

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SERIAL CHANGES OF SMOOTH MUSCLE CELL PHENOTYPES IN RAT URINARY BLADDER FOLLOWING PARTIAL OUTFLOW OBSTRUCTION

AIMS OF STUDY

Partial outflow obstruction of the urinary bladder induces the increased bladder weight characterized by a smooth muscle hypertrophy in addition to an increased collagen deposition within the bladder wall. Recently, in several smooth muscle organs such as cardiac artery or gall-bladder, the smooth muscle cells (SMC) can be classified pathomorphologically into three phenotypes; synthetic, contractile, and intermediate. The contractile SMC phenotype is often converted into the synthetic phenotype in response to various pathological conditions. While the function of the contractile SMC is essentially to contract, the synthetic SMC may play an important role in the replication, migration, and the elaboration or degradation of the extracellular matrix proteins. Contrast to the vascular smooth muscle, there has been few reports concerning SMC phenotypes in both normal and obstructed bladder. It is supposed that the conversion of contractile SMC phenotype into synthetic phenotype must be one of the most important clue to elucidate the mechanism of morphological and functional alterations in obstructed bladder dysfunction. The objective of the present study is to investigate the long-term change in bladder SMC phenotype following partial outflow obstruction.

MATERIAL & METHODS

Partial outflow obstruction was created in male Sprague-Dawley rats by tying a ligature around the proximal urethra in the presence of a 0.965 mm polyethylene tube. Urinary bladders were obtained 1, 3, 6, 10, 14, 20 and 30 weeks after obstruction, stained with H-E, Mallory-Azan and classified smooth muscle cells into non-contractile or contractile phenotype in electron-microscopically. And the ratio of non-contractile / contractile phenotype (nC/C ratio) was calculated. The expression amount of contractile protein (calponin) was measured in the remaining resected bladder specimens by the immunoblotting method.

RESULTS AND CONCLUSIONS

The mean weight of the bladder has been increased by 6weeks after outflow obstruction compared as sham operated bladder, and from 10 weeks to 30 weeks after outflow obstruction, kept on plateau. Macroscopically, marked thickening of the bladder wall was observed after outflow obstruction. Fibrosis and muscle-layer thickening were also observed. Sham operated bladder showed a negligible difference in % Fibrosis after surgery. While Obstructed bladder showed a significant decrease in % Fibrosis at 3 weeks, it showed same degree at 14 weeks after obstruction as compared to Sham operated bladder. Sham operated bladder showed a negligible difference in nC/C ratio, Obstructed bladder revealed a tendency to increase, but not statistically significant in proportion to the period of obstruction as compared to Control bladder. The expression amount of contractile protein (calponin) larger for the contractile type than for the synthetic type.