Aim of study

In humans the desire to void is influenced by urinary pH - the desire being experienced at lower bladder volumes when the urine is more acidic (1). Detrusor contractions can also be provoked in many patients by instillation of acidic solutions into the bladder (2). The working mechanisms for these effects remain to be clarified. The aim of the present experimental study in the rat was to modulate the micturition threshold by infusion of fluid at low pH and to identify associated changes in bladder afferent and efferent activity.

Methods

Thirteen female rats, anaesthetised by α-chloralose and paralysed by pancurone bromide, were used for the experiments. Micturition threshold volume was determined by repeated transurethral cystometries at low infusion speed (0.06 ml/min). Saline, titrated to pH 3, 4, 5, 6 and 7 by acetic acid, was used for infusions. Bladder afferent and efferent activity was recorded, simultaneously with cystometry, from exposed pelvic nerve branches to the bladder. After an initial equilibrium period, four control cystometries were performed with saline at pH 7. The different acidic solution were then tested in random order until at least 4 cystometries at each pH were obtained. A resting interval of at least 3 minutes, with the bladder open and empty, was interposed between successive cystometries.

Bladder pressure, afferent or efferent nerve activity together with the full-wave rectified and integrated nerve responses were continuously recorded on a HIOKI chart recorder and subsequently analysed off line with a PC based system. The following parameters were studied: afferent and efferent threshold volumes, micturition threshold volume and pressure, afferent activity at micturition threshold, peak afferent and efferent activity, bladder pressure at peak contraction, afferent pressure sensitivity. The used recording technique resolved primarily activity in myelinated Aδ afferents from bladder mechanoreceptors (3).

Results

A total of 509 cystometries were performed. There was a small gradual decrease in micturition threshold volume with acidic solutions from a mean volume 0.49 ml at pH 7 to 0.42 ml at pH 3. The change was only significant for the two lowest pH levels (pH 4 and 3; $p < 0.01$). At these low pH levels there was also a small decrease in mean bladder compliance (from 5.3 to 4.8 ml/ cm H2O; $p < 0.01$) and peak contraction pressure (from 41 to 39 cm H2O; $p < 0.5$). There was no detectable change in afferent or efferent pelvic nerve activity or in other measured parameters.

Conclusion

Cystometry with acidic solutions induced a significant decrease in the micturition threshold volume of anaesthetised rats. The decrease occurred without a detectable change in the firing properties of bladder Aδ mechanoreceptor afferents. It is proposed that proton sensitive bladder receptors with unmyelinated afferents were stimulated by the acidic solution and that the micturition reflex was facilitated by afferent inflow from such receptors.

Reference

(1) Neurourol Urodyn 16:396-397, 1997
(2) Neurourol Urodyn 9: 355-356, 1990
(3) Neurourol Urodyn 17:543-553, 1998

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DETRUSOR STIFFNESS. NEW INSTRUMENTATION FOR THE *IN VITRO* THE EVALUATION OF BLADDER CONTRACTION.

AIMS OF STUDY.

Current methods used in the evaluation of isometric bladder contraction involve the suspension of a strip of bladder into a chamber, tying one end of the tissue to a fixed point and the other to a force transducer. In the present study we introduce a new instrument for the measurement of bladder contraction obviating the need to tie the tissue. This instrument was used in the evaluation of bladder stiffness, produced by cholinergic stimulation of the rat bladder. The tissues used for these experiments were obtained from ovariectomized (OVX) and estrogen-treated (OVX+E) rats.

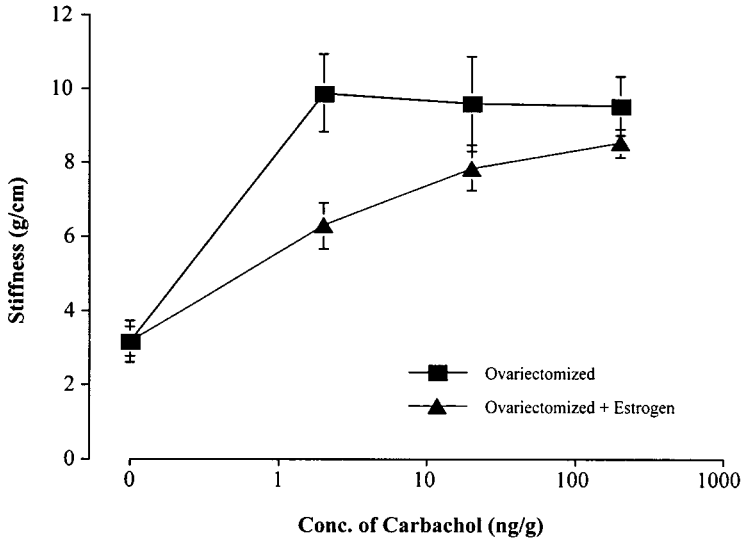
METHODS.

The stiffness biosensor was made up of a piezoelectric crystal (PZT) having 1mm in diameter and supported by a micromanipulator. The crystal was electrically driven at its resonance frequency by an oscillator. Upon contact with the tissue the resonance frequency of the PZT shifted in accord with tissue stiffness. This frequency shift, Δf, was calibrated to represent tissue stiffness in gm/cm.

Tissue segments, 50 mg in weight and approximately 5x5 mm^2 in size, were dissected from the bladder domes of 6 OVX and 6 OVX+E rats. The tissues were placed on a cotton gauze, soaked in Krebs solution, and placed under the biosensor so that three consecutive measurements could be taken. These initial measurements represent baseline stiffness. The response of the bladder was measured when high [K$^+$] and increasing doses of Carbachol 2,20,200 ng/kg were directly applied onto the surface of the tissues. Three measurements were taken after the addition of each dose. Dose response curves were generated for the stiffness of the OVX and OVX+E groups.

RESULTS

The results show that the biosensor was able to produce consistent and reliable measurements of bladder stiffness under control conditions. Figure 1 shows a dose response curve of the relationship of bladder stiffness to Carbachol concentration. As indicated stiffness is shown to increase significantly following the addition of Carbachol. The response to increasing doses of the stimulant was markedly different between the two groups of rats, indicating that the biosensor possesses sufficient sensitivity for detecting variations in tissue stiffness.



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+