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FUNCTIONAL PROPERTIES AND PUDENDAL NERVE STIMULATION OF AN ISOLATED GUINEA-PIG URETHRA PREPARATION.

Aims of Study

The female guinea-pig urethra is structurally similar to the human in that it comprises of a prominent outer striated muscle sheath, which encapsulates the less abundant inner smooth muscle. The muscle cells of this outer layer are thought to be entirely of the slow twitch variety and are thus capable of exerting prolonged tone (1). The guinea-pig is consequently a useful comparative model for human urinary incontinence, as it remains functional with its nerves intact within an isolated organ bath preparation.

Methods

Female Dunkin-Hartley guinea-pigs, weighing 300-400g, were sacrificed by cervical dislocation. The lower body was taken following complete transection of the thoracic spinal cord at level T11. Carefully dividing the pubic symphysis allowed access to the underlying pudendal nerves. Both pudendal nerves were carefully dissected from the caudal end of the urethra back to the spinal cord, cleaned and tied together with silk thread. Excess fat from the bladder base and urethra was removed, along with the vagina and rectum. The preparation was immediately suspended vertically for tension (mainly longitudinal smooth muscle) and intra-lumenar pressure (predominantly circular striated muscle) recording in a 40ml perfusion organ bath. Drugs were applied in the perfusate and electrical field stimulation (EFS) of the pudendal nerves achieved via two platinum ring electrodes. For histochemical studies, urethrae underwent staining for NADPH-diaphorase activity using established methodology.

Results

EFS of the pudendal nerves (stimulation parameters: 0.1ms pulses at 70V and 1Hz repeat stimulation) evoked intra-lumenar pressure increases, which were unaffected by hexamethonium (100µM) and completely blocked by tubocurarine (10µM). Application of phenylephrine increased urethral tension in a dose dependent manner. Histological studies showed nerves staining positive for NADPH-diaphorase activity in the striated muscle layers of the guinea-pig urethra. In addition, cumulative application of SNP relaxed the phenylephrine-contracted urethrae in a dose dependent manner. With addition of LNOArg (100µM) and zaprinast (10µM) having no effect on the pressure increases evoked by EFS of the pudendal nerve.

Conclusions

The failure of hexamethonium to inhibit the intra-lumenar pressure increases suggests the smooth muscle component of the urethra has no function in the twitch contraction evoked by EFS of the pudendal nerve. Conversely, the contractions were completely blocked with tubocurarine signifying somatic innervation of the striated muscle of the guinea-pig urethra. Histological studies show evidence of NOS containing nerves in the striated muscle layers of the urethra and the relaxant response of the tissue to SNP demonstrates NO might play a role. However, inhibiting NOS and cGMP degradation had no effect on the EFS evoked contractions suggesting NO and the cGMP pathway probably have no modulatory effect on the neurogenic contractions of the guinea-pig urethral striated muscle.

References

(1) Gosling, J.A., Dixon, J.S. & Humpherson, J.R. (1983). Functional anatomy of the urinary tract. An integrated text and coloured atlas; 1st ed., Gower Medical Publishing.