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NON ADRENERGIC, NON CHOLINERGIC, NON NITRERGIC RELAXATION IN PIG URINARY BLADDER NECK: A THERAPEUTICAL APPROACH IN TYPE III STRESS URINARY INCONTINENCE.

Hypothesis / aims of study: Since the urinary bladder neck together with the proximal urethra form the urine outflow region of the bladder, knowledge of the transmitters involved in the control of smooth muscle tone of such structure is essential for understanding the mechanisms involved in the maintenance of urinary continence. Nitric oxide (NO) and peptides, such as pituitary adenylate cyclase-activating polypeptide (PACAP) are involved in NANC inhibitory neurotransmission of the bladder neck producing smooth muscle relaxation through neuronal or non-neuronal mechanisms. In addition to the above mentioned agents, a large non adrenergic non cholinergic (NANC) nerve stimulation-evoked relaxation resistant to NO synthase (NOS) or VIP/PACAP receptor inhibitors has also been described, thus indicating the involvement of other mediator(s) in such relaxations. The aim of the present study has been to investigate possible mechanisms involved in NO-independent NANC inhibitory neurotransmission in pig urinary bladder neck.
Study design, materials and methods: Urothelium denuded strips 4-6 mm long and 2-3 mm wide were suspended horizontally with one end connected to an isometric force transducer (Grass FT 03C) and the other one to a micrometer screw, in 5 ml organ baths containing PSS at 37^{o} C gassed with carbogen (95% O_2 and 5% CO_2) to obtain a final pH of 7.4. The signal was continuously recorded on a polygraph (Graphtec Multicorder MC 6621). Passive tension of 2 g was applied to the strips and they were allowed to equilibrate for 60 min. On 1 μM phenylephrine (PhE)-induced tone, relaxations to electrical field stimulation (EFS) was performed by delivering rectangular pulses (1 ms duration, 1-16 Hz, 20 s trains, with constant current output adjusted to 75 mA), at 4 min intervals, from a Cibertec CS20 stimulator.
Results: Noradrenergic neurotransmission, muscarinic receptors and (NOS) were blocked. Under these conditions the relaxations evoked by EFS at 1 Hz, 2 Hz, 4 Hz, 8 Hz and 16 Hz (as percentage of the maximal relaxation) were of 5±4 %, 27±6 %, 59±6 %, 87±4 % and 100±0 %, respectively, these responses being reproducible in a second nerve stimulation curve. TTX, a neuronal voltage-gated Na^+ channels blocker, abolished the relaxations indicating their neurogenic character. However, ODQ, iberitoxin, apamin, glibeclamide, cAMPS-Rp and [Ala^{32}]H2B(29-35), inhibitors of soluble guanylyl cyclase, large and small Ca^{2+}-activated K^+ channels, ATP -dependent K^+ channels, cAMPc-dependent protein kinase (PKA) and cGMP-dependent protein kinase (PKG), respectively, failed to modify the neural relaxations.
Interpretation of results
These results suggest that non nitrergic NANC inhibitory neurotransmission produces relaxation of smooth muscle in the pig bladder neck, through a mechanism independent of the PKA or PKG pathways or postjunctional K^+ channels.
Concluding message
The identification of the involved mechanisms in non nitrergic NANC inhibitory neurotransmission is essential for treatment of the urinary incontinence produced by intrinsic sphincteric deficiency.
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References

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What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**No**
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