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THE ROLE OF THE MUCOSA IN MEDIATING SPONTANEOUS CONTRACTIONS OF THE PIG URINARY BLADDER

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HYPOTHESIS / AIMS OF STUDY

Normal bladder function requires co-operative interaction of several cell types. Isolated detrusor muscle generates nerve-evoked contractions, regulated by the release of transmitters, as well as spontaneous contractions (SCs), associated with spontaneous action potentials. However, it appears that the mucosa (urothelium and lamina propria) influences spontaneous contractile activity and associated intracellular Ca2+ transients recorded from the bladder wall (1,2). When isolated, the mucosa can also develop spontaneous and agonist-induced contractile activity and when left intact with the detrusor layer, greatly augments the spontaneous contractile activity (3). What is unclear is if the mucosa interacts with the detrusor via release of diffusible agents or through cell-to-cell contact. The aim of this study was to investigate the nature of this interaction by measuring SCs from detrusor preparations with and without an adjacent mucosa, using tissue from a large animal (pig) bladder with an architecture similar to that of the human bladder.

STUDY DESIGN, MATERIALS AND METHODS

Female pig (Sus scrofa domestica ~6-months old) bladders obtained from a local abattoir were placed in cold Krebs bicarbonate (KB) solution (mM: NaCl 118.4, NaHCO3 24.9, KCl 4.7, CaCl2 1.9, MgSO4 1.15, KH2PO4 1.15, glucose 11.7). From each bladder dome, four sets of longitudinally-orientated preparations were prepared. These were: (a) intact (detrusor + mucosa); (b) denuded (detrusor with mucosa removed); (c) mucosa alone; (d) reconstructed (denuded with previously isolated mucosa placed on top). Preparations were tied between a fixed hook and an isometric force transducer, maintained under a fixed (20 mN) load in KB solution at 37°C for 45 min. SCs were recorded and assessed during the final 15-min of the equilibration period. The amplitude (μN/mg tissue) and frequency (number of events in 5-min) of SCs were recorded and compared between the four different preparations. All data are expressed as the medians (25,75% interquartiles), n = number of bladder strips. Statistical analyses were carried out by Kruskal-Wallis rank sum test, followed by Wilcoxon non-parametric tests.

RESULTS

The basal SCs were detected in 100% of mucosa, intact and reconstructed pig bladder strips. However, only 30% of denuded strips demonstrated basal SCs. The amplitude and frequency of basal SCs were significantly smaller in denuded strips vs. all other strip types (Figure 1). The highest amplitude of SCs was detected in mucosa strips (Figure 1A). There was no significant difference in the amplitude or frequency of SCs between intact vs. reconstructed strips, demonstrating that a functional physical connection between the layers was not needed for generation of SCs.

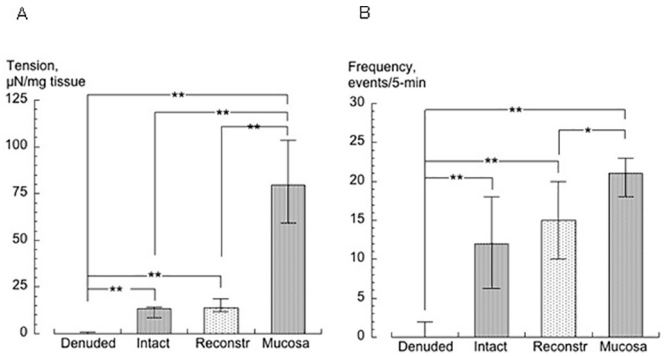
INTERPRETATION OF RESULTS

The contractile properties of the bladder mucosa have been previously described and it is speculated that phasic activity of intact bladder strips may be influenced by this layer (1,2,3). Our study demonstrated that the pig bladder detrusor alone, similar to guinea pig detrusor, has very little intrinsic ability to generate spontaneous activity and the interaction between mucosa and detrusor is required for generation of SCs. Dissecting the mucosa away from the muscle and then reattaching it to the detrusor restores spontaneous activity. This implies that there is a diffusible factor between the mucosa and the detrusor modulating the spontaneous activity and cellular/physical connection between these two layers is not required for generation of SCs.

CONCLUDING MESSAGE

Spontaneous activity of pig bladder originates from the mucosal layer possibly through the release of a diffusible factor which acts on the underlying detrusor to generate SCs. Further studies are needed to identify the source and nature of this diffusible factor.

FIGURE 1



SCs in pig bladder wall preparations. A: amplitude of SCs normalised to preparation weight C: frequency of SCs in denuded, intact, reconstructed (reconstr) & mucosa strips (all n = 9). Data are median (25,75% interquartiles; *p < 0.05, **p < 0.01, Wilcox tests)

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