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LETTERS)**COMPARISON OF THE EFFECTS OF POTASSIUM CHLORIDE IN
THE HUMAN AND PORCINE LOWER URINARY TRACT**

Aim of Study: Previously, the pig has been shown to be a suitable model for studying the properties of lower urinary tract (LUT) smooth muscle, sharing many characteristics with the human. An additional advantage of the use of porcine tissue is that it is readily available.

The effect of increasing concentrations of potassium chloride on smooth muscle from various regions of the porcine LUT was investigated. The results were then compared in a qualitative and quantitative fashion with the effect of potassium chloride on isolated human LUT smooth muscle strips.

The aim of this study was to investigate the potential of the pig as an appropriate model for comparison of functional properties in the LUT.

Methods: Intact porcine detrusor and urethra were excised from freshly slaughtered female Large White pigs (approximately 60kg) in a local abattoir and transported to the laboratory in cold Krebs solution (ca 4°C). Normal human detrusor and urethra were obtained from cadaveric organ donors and transported to the laboratory in cold Krebs solution. Subsequently, LUT samples were dissected into anatomically distinct regions, before smooth muscle strips (1x1x5mm) were obtained with the use of a binocular dissection microscope. In both species, detrusor strips were dissected from the dome region. In the pig (total urethral length of approximately 8cm), the proximal portion of the urethra was divided into 1cm regions from the bladder neck down (Segments 1,2,3,4 were used - Segment 1 being distal to the bladder neck) and smooth muscle strips were dissected from both the circular and longitudinal muscle coats. In the female human (total urethral length of approximately 4cm), the whole urethra was divided into 3 equal regions (designated proximal, mid and distal) and, as in the pig, both longitudinal and circular smooth muscle strips were dissected. Strips from various regions and orientation were obtained from a single specimen. All strips were suspended at an initial tension of 1 gram in 0.2ml superfusion organ baths using silk ligatures. Strips were constantly perfused with carboxygenated Krebs solution (37°C, pH 7.4) and were allowed to equilibrate for a period of up to 90 minutes. The effect of 2 minute applications of increasing concentrations of potassium chloride (25-126mM) was

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studied. The desired potassium chloride concentration was obtained by equimolar replacement of sodium chloride solution with potassium chloride (KCl) in Krebs solution.

Results: Responses to increasing concentrations of KCl were obtained for female human (n=15, N=2) and pig (n=16, N=10) detrusor smooth muscle strips. As expected, concentration dependent contractile responses were observed in both the human and porcine detrusor. The response to a 2 minute application of 126mM KCl in porcine strips resulted in a contraction of magnitude 4.41 ± 0.69 g/mg. A contractile response of 3.64 ± 0.63 g/mg was observed in human tissue under identical conditions. Similarities were observed, both in terms of nature and magnitude of response in both species.

In contrast to the detrusor, biphasic responses were observed in the porcine urethra that consisted of a transient contraction followed by a persistent relaxation varying in magnitude with increasing concentrations of KCl. The relaxatory response to KCl has been observed previously (1). The relaxation became a more prominent component of the total tissue biphasic response upon descent of the urethra. A 2 minute application of 86mM KCl in Segment 1 circular smooth muscle strips (n=16, N=13) caused a contraction of 0.64 ± 0.09 g/mg followed by a relaxation of 0.13 ± 0.03 g/mg of tissue. In circular strips from Segment 4 (n=17, N=13), a contractile response of 0.17 ± 0.06 g/mg and a relaxation of magnitude 0.16 ± 0.04 g/mg was recorded under identical conditions. The relaxation component of the biphasic response also increased in magnitude with increased application time of KCl.

In the female human urethra, phasic, biphasic and relaxant responses were also observed in response to short applications of potassium chloride.

Conclusion: This preliminary study illustrates functional differences between detrusor and urethral smooth muscle. In addition, similarities between porcine and human lower urinary tract smooth muscle response to potassium chloride have been observed. This supports the use of the pig as a comparative model for human lower urinary tract functional studies. More detailed comparison between porcine and human tissue may aid identification of differences in ion channel properties between the detrusor and urethra that could be harnessed to provide therapeutic alleviation of urinary incontinence.

References:

1. High potassium solution induces relaxation in the isolated pig urethra. *J. Physiol.* 430, 118P, 1990