

SPONTANEOUS CONTRACTIONS OF THE PIG BLADDER: EFFECT OF THE ATP-DEPENDENT POTASSIUM CHANNEL OPENER CROMAKALIM AND INFLUENCE OF THE UROTHELIUM.

Hypothesis / aims of study

Spontaneous contractions of the bladder have been recently considered to be important in the sensation of bladder filling. It is known that ATP-dependent potassium (K_{ATP}) channel openers have an inhibitory effect on these spontaneous contractions (1). The urothelium is also thought to release a factor that inhibits detrusor contractions (UDIF) (2), and although this has yet to be identified, it may also inhibit spontaneous contractions. The present study investigates the influence of the urothelium on the inhibitory responses of the K_{ATP} channel opener, cromakalim, on spontaneous contractions of isolated strips from the trigone and dome of the pig bladder.

Study design, materials and methods

Strips of trigone and dome were taken from pig bladders and mounted in organ-baths containing gassed Krebs-bicarbonate solution at 37°C. In some strips the urothelium was carefully removed using scissors. Spontaneous activity was allowed to develop, and following this cumulative concentration response curves to cromakalim were obtained (100nM - 100µM). The frequency and amplitude of spontaneous contractions were recorded before and after the addition of cromakalim and the percentage decrease following cromakalim calculated. An unpaired Student's t-test or Mann-Whitney U-test was used for statistical analysis, with a p-value of <0.05 considered statistically significant.

Results

Spontaneous contractions were observed in all strips isolated from the trigone (n=12) and dome (n=12) of pig bladders. For dome, the time after set-up that was needed for the spontaneous contractions to appear was less than 15 minutes for those with urothelium, and usually 30 to 60 minutes for those without urothelium. The spontaneous contractions of trigone appeared within 15 minutes after set-up regardless of the presence or absence of urothelium. Cromakalim reduced the frequency of spontaneous contractions in strips of dome in a concentration-dependent manner; $-8.6 \pm 6.7\%$ (mean \pm SEM), $5.9 \pm 10.4\%$, $41.8 \pm 11.7\%$ and $95.0 \pm 5.0\%$ at 100nM, 1µM, 10µM and 100µM, in the presence of a urothelium (n=6) and $-2.7 \pm 4.6\%$, $32.9 \pm 9.4\%$, $96.6 \pm 3.2\%$ and 100% respectively in the absence of a urothelium (n=6). The response to 10µM cromakalim was significantly smaller (p=0.0022) in the presence of an intact urothelium.

The amplitude of spontaneous contractions in strips of dome was also reduced by cromakalim and again the reductions were significantly smaller if the urothelium was present, cromakalim reducing the amplitude of contractions by $11.0 \pm 14.5\%$ at 1µM and $50.7 \pm 7.9\%$ at 10µM in the presence of urothelium compared with $67.0 \pm 12.0\%$ (p=0.0139) and $97.6 \pm 2.4\%$ (p=0.0022) for these contractions in the absence of the urothelium.

In contrast, in the strips of trigone, the urothelium had no influence on inhibition of spontaneous contractions by cromakalim. The K_{ATP} channel opener inhibited the frequency and the amplitude of spontaneous contractions equally in tissues with and without an intact urothelium.

Interpretation of results

Spontaneous contractions were observed in all strips of pig bladder, suggesting that spontaneous contractions are a normal in-vitro phenomenon. The delay of the appearance of spontaneous contraction in the strips of dome without urothelium suggests that the urothelium and suburothelial structures may have an important role in the generation of the spontaneous contractions of the dome. In trigone strips, there were no differences in the time that the spontaneous contractions developed between strips with and without urothelium, which suggests that trigone differs from dome with regards to the mechanism of the generation of the spontaneous contractions.

Unexpectedly, the strips of dome with urothelium showed a significant resistance to the inhibitory actions of cromakalim, compared to those without urothelium. The reason for this is unknown, but it is unlikely to be due simply to a barrier effect of the urothelium as no differences were observed in the responses to cromakalim in trigone strips with and without urothelium.

Concluding message

Both trigone and dome of the pig bladder show spontaneous contractions, which are inhibited by cromakalim. In dome, this inhibition is reduced in the presence of an intact urothelium and suburothelium, whereas in trigone these structures appear to have no influence.

References

1. Buckner SA, et al: Br J Pharmacol 135: 639, 2002.
2. Hawthorn MH, et al: Br J Pharmacol 129: 416, 2000.

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DISCLOSURES: NONE

ANIMAL SUBJECTS: This study did not follow the guidelines for care and use of laboratory animals because the pig tissues used for the experiments were got from the local abattoir.