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INHIBITORY EFFECTS OF B-ADRENOCEPTOR AGONISTS ON DETRUSOR CONTRACTION INVOLVE THE B3-ADRENOCEPTOR IN PIG BLADDER DOME

Hypothesis / aims of study

Recently, the function of the bladder urothelium has become a focus of interest. Although it has previously been regarded as a passive barrier, it is now thought that the urothelium releases several neurotransmitters and is involved in the control of bladder function. However, the role of the urothelium in bladder responses to β-adrenoceptor agonists is not yet clear. We have recently shown that β-adrenoceptor agonists have a greater inhibitory effect on contraction of the detrusor when the urothelium is intact [1] and the β_3-adrenoceptor subtype appears to be involved in this effect [2]. The aim of the present study was to confirm the role of the β_3-adrenoceptor subtype using subtype selective agonists and antagonists.

Study design, materials and methods

Paired longitudinal strips of bladder dome were isolated from fresh pig bladders. The urothelium was removed from 1 strip per pair and the strips mounted in tissue baths in gassed Krebs solution at 37°C. The inhibitory effects were studied by obtaining carbachol-response curves in the absence and presence of β-adrenoceptor agonists (dobutamine, salbutamol, or BRL37344; β_1, β_2 and β_3 selective respectively). In separate experiments the inhibitory effects of isoprenaline (non-selective β-adrenoceptor agonist) were studied following incubation with β-adrenoceptor antagonists (propranolol, CGP20712, ICI-118, 551, or SRL59230A; non selective, β_1, β_2 and β_3 selective respectively). Results are mean ± SEM and paired Student's t-test was used for statistical analysis.

Results

Contractile responses to carbachol were depressed by 44.6±2.7 % in the presence of the urothelium and the potency (pEC_{50}) of carbachol was also significantly reduced ($p<0.05$) in the presence (5.45±0.05) compared with the absence (5.70±0.06) of the urothelium (n=94). In inhibition experiments using β-adrenoceptor agonists, the agonists caused rightward parallel shifts of the carbachol-response curves. There was a greater shift with 10μM BRL37344 in the presence of the urothelium than in the absence of the urothelium (n=8; mean shift: 3.53±0.46 vs 2.02±0.29, $p<0.05$). However this was not observed with 10μM dobutamine (n=7; mean shift: 1.31±0.09 vs 1.39±0.19) and 10μM salbutamol (n=6; mean shift: 2.53±0.67 vs 2.39±0.40). The non-selective β-adrenoceptor agonist isoprenaline (10 μM) produced a greater shift in the presence of the urothelium than in the absence (n=8; mean shift: 4.55±0.63 vs 3.18±0.33, $p<0.05$), and this was still observed in tissues pre-incubated with 1μM propranolol (n=6; mean shift: 3.12±0.59 vs 1.74±0.17, $p<0.05$), 1μM CGP20712 (n=7; mean shift: 4.38±0.77 vs 2.90±0.62, $p<0.05$) and 1μM ICI-118, 551 (n=6; mean shift: 3.20±0.26 vs 1.92±0.15, $p<0.05$). However, this difference was not observed when tissues were pre-incubated with 1μM SRL59230A (n=5; mean shift: 1.85±0.32 vs 1.86±0.19).

Interpretation of results

The β_3 selective agonist BRL37344 was the only selective agonist seen to have a greater inhibitory effect on detrusor contraction when the urothelium was intact. This implies a role for the β_3 -adrenoceptor. This was confirmed by the effect being antagonised only by the selective β_3-adrenoceptor antagonist SRL59230A.

Concluding message

These data suggest that β_3-adrenoceptors are involved in mediating the inhibitory effects of β-adrenoceptor agonists via the urothelium in pig bladder dome.

References

[1] BJU Int (2007) 99; 669-673
[2] Eur Urol (2007) 6; Suppl 40

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ANIMAL SUBJECTS: This study did not follow the guidelines for care and use of laboratory animals because We obtained pig bladder tissues from a local abattoir.