Histamine H1 and H2 receptors as regulators of urinary bladder urothelium/lamina propria and detrusor contractile activity

Zane Stromberga, Russ Chess-Williams, Christian Moro

Centre for Urology Research, Bond University, Australia

Background: The mechanisms underlying bladder contractile disorders, such as overactive bladder, are not fully understood. It is apparent that acetylcholine release is involved, yet other mediators and regulator chemicals may also influence detrusor contraction. As such, there is a particular interest in identifying which receptors other than muscarinic are involved in modulating spontaneous contractile activity. This study aimed to identify the specific influence of the H1, H2, H3 and H4 histamine receptors on urothelium/lamina propria and detrusor contractile activity.

Methods: Strips of porcine urothelium/lamina propria and detrusor were mounted in gassed Krebs-bicarbonate solution at 37°C and responses to histamine obtained in the absence and presence of selective receptor antagonists. Data analysis of the responses was performed using paired Student's *t*-tests.

Results: The urothelium/lamina propria contracted in the presence of histamine (100 μ M) by 1.05 ± 0.20 g and the frequency of spontaneous contractile activity was increased by 1.53 ± 0.38 cycles per min (cpm, $n = 26$). Pyrilamine (30nM, H1 antagonist) inhibited these contractile responses ($p < 0.01$, $n = 6$) and did not increase the frequency of spontaneous contractions ($p < 0.01$, $n = 6$, Table 1). In the presence of cimetidine (1 μ M, H2 antagonist) maximal contractions to histamine were enhanced ($p = 0.05$, $n = 8$). Although thioperamide (1 μ M, H3 and H4 antagonist) initially produced a significant increase in contractions ($p = 0.03$, $n = 6$), selective antagonism revealed no influence of H3/H4 receptors. In detrusor preparations, H1 receptors were responsible for the majority of the contraction to histamine ($p < 0.05$, $n = 8$), with contractions not influenced by antagonism of H2, H3 or H4 receptors.

Conclusions: Histamine produces a contractile response in the urothelium/lamina propria and detrusor via the H1 receptor and relaxation via the H2 receptor in the urothelium/lamina propria. This data identifies these systems as potential targets in future therapeutic treatments for overactive bladder or other bladder contractile diseases.