

DISTRIBUTION OF TYPE 2 AND 3 MUSCARINIC RECEPTORS IN THE HUMAN BLADDER

Aims of Study

Muscarinic type 2 (M2) and muscarinic type 3 (M3) appear to be the main receptors present in human and pig bladders. These muscarinic receptor subtypes have been identified by using radioligand binding and functional studies. The relative amounts of these 2 receptors have been quantified which have showed the M2:M3 ratio being 3:1. The M3 receptor is thought to be the main receptor involved in producing contraction of the detrusor smooth muscle.

The aim of this study is to investigate the position of the M2 and M3 receptors in the human bladder and from this to determine possible effects stimulating these receptors.

Methods

Dome bladder biopsies were taken from women with a urodynamic diagnosis of idiopathic detrusor overactivity. Biopsies were fixed in 4% paraformaldehyde put into 7% sucrose overnight flash frozen in OCT and stored at -80C. 8-10 µm sections were cut and stained using immunohistochemical techniques using a M2 antibody (Rabbit IgG) and the M3 antibody (Goat polyclonal IgG, Santa Cruz). An HRP enzyme linked antibody was used to visualise the receptors and developed with DAB. These were serial sections. Another section was stained with haematoxylin and eosin to allow identification of the urothelium, lamina propria and the detrusor muscle layer. The areas of the lamina propria and detrusor muscle were measured and the numbers of receptors in the 2 areas were counted manually to obtain a density of the muscarinic receptor subtypes in these two histological areas.

Results

Bladder biopsies of 5 women were studied. The M2R were found in the lamina propria in dense compact forms as spiral structure. The M3R were found diffusely in the detrusor muscle.

Receptor	Mean No per Area-Lamina propria	Mean No per Area-detrusor muscle	Total density
M2	1849	3087	4937
M3	1380	1521	2901

Table 1 : Relative density of the M2 and M3 receptors in the bladder

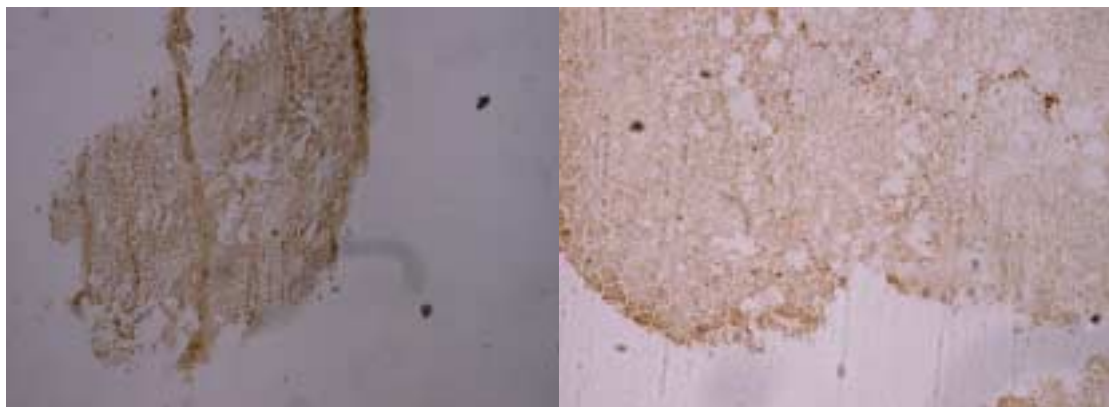


Fig 1 : M3R in detrusor muscle

Fig 2: M2R in lamina propria

The ratio of the M2 : M3 receptors was 1.7 : 1 in bladder biopsies but the pattern of the receptors was very different with the M2R in string like patterns in the lamina propria (fig2) and diffuse receptors in the detrusor muscle (fig 1).

Conclusions

Muscarinic receptors type 2 and type 3 have different patterns in the bladder muscle which suggest very different modes of action. The position of the M2 receptors suggest an alignment with another structure in the lamina propria. M2 receptors do have a greater density than the M3 receptors.