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MUSCARINIC RECEPTORS SUBTYPES M2 AND M3 IN HUMAN URINARY BLADDER DISORDERS AND THEIR CLINICAL CORRELATIONS

Hypothesis / aims of study

The cellular localization and role(s) of different muscarinic receptors in human urinary bladder syndromes is uncertain. We have studied the muscarinic receptor subtypes M_2 and M_3 in the human urinary bladder, and related changes in the receptor density of patients with detrusor overactivity, painful bladder syndromes and controls to clinical measures such as urinary frequency and urgency.

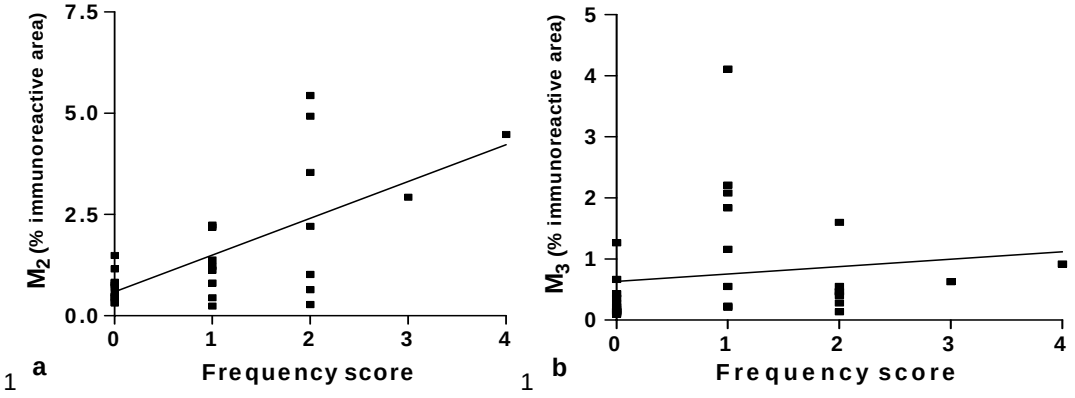
Study design, materials and methods

Bladder specimens obtained from patients with painful bladder syndrome (PBS, n=11), idiopathic detrusor overactivity (IDO, n=12), and asymptomatic microscopic hematuria (controls, n=16), were immunostained using specific antibodies to muscarinic receptor subtypes M_2, M_3 and vimentin (a marker for myofibroblasts). Results of immunostaining were quantified with computerized image analysis, and were correlated with the clinical dysfunction (Frequency and Urgency scores).

Results

M_2- and M_3-immunoreactivity was observed in the urothelium, nerve fibres, and detrusor layers: in addition, strong "myofibroblast-like" cell staining, similar to vimentin, was present in the suburothelial region and detrusor muscle. A significant increase in the sub-urothelial myofibroblast-like M_2-immunoreactivity was seen in both PBS (P=0.0062) and IDO (P=0.0002), and myofibroblast-like M_3–immunoreactivity in IDO (P=0.0122), with a trend in PBS. The M_2- and M_3-immunoreactivity significantly correlated with the Urgency score (P=0.0002 and 0.0206 respectively) (fig c and d), and M_2-immunoreactivity with the Frequency Score (P=0.0029)(fig a). No significant difference was seen in the M_2-, M_3 - urothelial and detrusor or vimentin- immunostaining.

Fig (1a) frequency score compared with M2 immunoreactive area (1b) M3 immunoreactive area



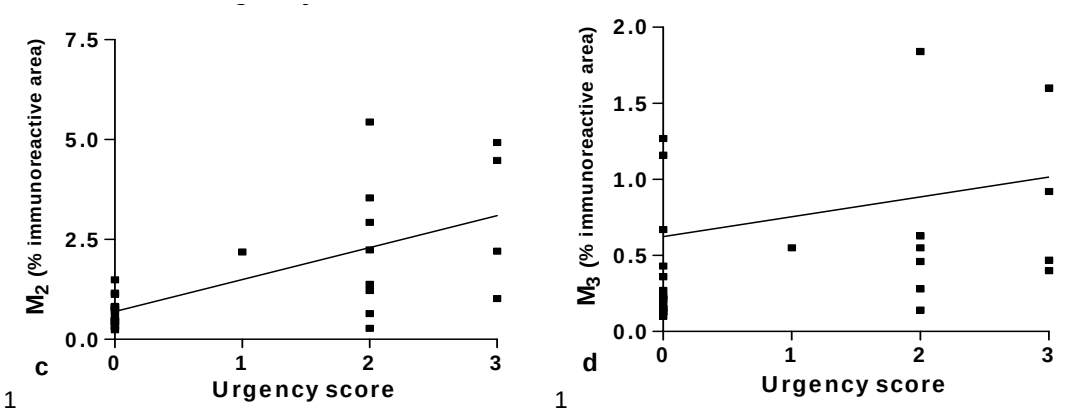
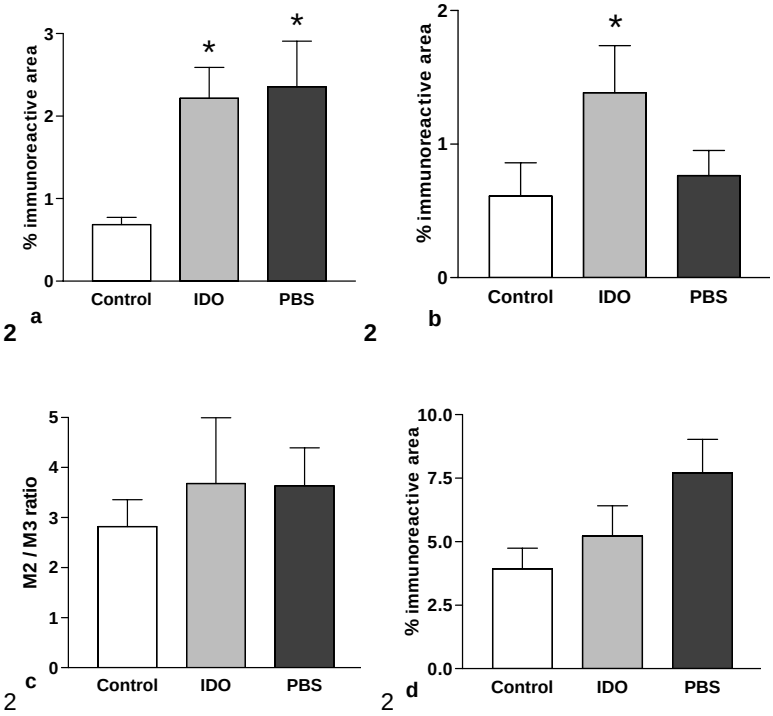


Fig (1c) urgency score correlated against M2 immunoreactive area (1d) against M3 immunoreactive area



Bar charts showing the relative % area (mean ±SEM) of **(2a)** M_2-immunoreactive myofibroblasts, **(2b)** M_3-immunoreactive myofibroblasts**, (2c)** M_2 / M_3 Ratio (%)and **(2d)** Vimentin staining in control (n=16), IDO (n=12) and PBS (n=11) groups**.**

Interpretation of results

This study demonstrates the cellular localisation and distribution of muscarinic receptors M_2 and M_3 in the human urinary bladder disorders. The increase in M_2-and M_3-immunostaining in myofibroblast-like cells in clinical bladder syndromes, and correlation with clinical scores, suggests a potential role in pathophysiological mechanisms and the therapeutic effect of anti-muscarinic agents.

Concluding message

Muscarinic receptors do correlate with clinical symptoms in detrusor overactivity and painful bladder syndrome. M2 and M3 immunoreactivity correlate with urinary frequency and only M2
Significantly correlate to urgency

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