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THE FIRST INDICATION OF PHOSPHODIESTERASE TYPE 2 PRESENCE IN THE GUINEA PIG BLADDER

Hypothesis / aims of study

Phosphodiesterase inhibitors type 5 (PDE5i), have recently been suggested to have positive effects on the treatment of LUTS and DO [1,2]. Besides the well known PDE5 inhibitors, PDE2 selective inhibitors (PDE2i) have recently become available for clinical studies, showing positive effects on memory function. Provided that the PDE2 enzyme is expressed in the bladder, the study of the effect of PDE2i on bladder function would be very interesting. Antibodies against PDE2 are not available and the distribution of PDE2 in the bladder has never been demonstrated prior to this study.

Study design, materials and methods

Since antibodies to PDE2 enzyme are not available, we used a novel indirect technique, to study the localisation of PDE2, by visualizing the product of inhibition of PDE2, namely cGMP. Bladders of 12 guinea pigs, were dissected, and treated in wells containing 2 ml Krebs’ solution and 1 μM of the PDE-2 selective inhibitor Bay 60-7550, at 36°C for 30 min. Tissues were then stimulated with 100 μM of the Nitric oxide (NO) donor (diethylamine-NONOate) for 10 min. The tissues were then snap frozen and 10 μm sections cut. Sections were examined for cGMP immuno-reactivity and co-stained for a non-specific nerve marker (PGP9,5).

Results

Comparing bladder sections of NO stimulated guinea pig bladders and bladders treated with a PDE2i after NO stimulation, we were able to study the site of action of the PDE2i in the guinea pig lateral wall.

As shown in Figure 1A, PDE2i inhibits cGMP breakdown the most in the, urothelial and suburothelial layers as well as the nerve fibers. In the outer muscle layers of lateral wall, cGMP is mainly expressed in the intermuscle interstitial cells and the nerve fibers, indicating the presence of PDE 2 enzyme activity (fig. 1B).
Interpretation of results

Our study shows the distribution of PDE2 in the bladder. PDE2 is shown to be present in the urothelium and bladder muscle layers of the guinea pig. PDE2 activity is mainly located on umbrella cells and interstitial cells of the suburothelium. In the outer muscle, both the interstitial cells and some nerve fibers show PDE2 activity. This observation suggests the involvement of the NO-mediated cGMP system in the regulation of bladder activity, both through interstitial cells as well as through the nervous system.

Concluding message

Knowledge of the presence and the location of the PDE2 activity in the bladder is the first step towards physiological experiments required for studying the possible role of PDE2 in modulating bladder activity and possibly in the pathophysiology of urgency symptoms as in the overactive bladder syndrome.

References


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2. The BJU International Collaborative Research award 2007

Is this a clinical trial? No

What were the subjects in the study? ANIMAL

Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained? Yes

Name of ethics committee Maastricht University Animal Ethical Committee.