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# THE EFFECTS OF FLAVOXATE HYDROCHLORIDE ON THE VOLTAGE-DEPENDENT L-TYPE CA2+ CURRENTS IN THE HUMAN URINARY BLADDER

Hypothesis / aims of study

Flavoxate Hydrochloride has been widely utilized in order to treat urinary urge incontinence and pollakisuria for approximately three decades. Flavoxate is well-known to modulate the control of micturition in the central nerve system. In contrast, some reports have suggested that flavoxate may be a pasmolytic agent for detrusor smooth muscles. However, the precise mechanisms regarding flavoxate-induced detrusor relaxation still remain to be elucidated. In the present study, we investigated the effects of flavoxate on the voltage-dependent nifedipine-sensitive inward $Ba^{2+}$ currents.

Study design, materials and methods

The effects of flavoxate on the voltage-dependent nifedipine-sensitive inward $Ba^{2+}$ currents in human detrusor myocytes were investigated using patch-clamp methods. Tension measurements were also performed to study the effects of flavoxate on high $K^{+}$ solution-induced contraction in the human urinary bladder.

Results

Flavoxate caused a concentration-dependent relaxation of the $K^{+}$-induced contraction in the human urinary bladder. In human detrusor myocytes, flavoxate inhibited the peak amplitude of voltage-dependent nifedipine-sensitive inward $Ba^{2+}$ currents in a concentration-dependent manner. Flavoxate suppressed the peak amplitude of the voltage-dependent nifedipine-sensitive inward $Ba^{2+}$ currents in a voltage-dependent manner. Flavoxate shifted the steady-state inactivation curve of the voltage-dependent $Ba^{2+}$ currents to the left at a holding potential of -90 mV. Immunohistochemical studies indicated the presence of the $a_{1C}$ subunit protein, which is composed of human L-type $Ca^{2+}$ channels.

Interpretation of results

We have been able to demonstrate that flavoxate possesses a direct $Ca^{2+}$ antagonistic action on human detrusor in addition to the actions as a modulator of the micturition centre in CNS.

Concluding message

We have been able to demonstrate that flavoxate caused a detrusor relaxation through the inhibition of L-type $Ca^{2+}$ channels in human detrusor.