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DIMETHYL SULFOXIDE (DMSO) INDUCES RELAXATION OF HUMAN DETRUSOR MUSCLE

Aims of Study

Dimethyl sulfoxide (DMSO) is one of the most common solvents used in biological studies and as a vehicle for drug therapy. DMSO has been used in several human therapeutic situations and has been approved for intravesical instillation in interstitial cystitis (IC), a chronic, severely debilitating disease of the urinary bladder. DMSO, an agent that provides symptomatic relief in many patients with IC works via an unknown mechanism. The present investigation was undertaken to determine the action of DMSO on detrusor smooth muscle for its effects on 1) high potassium induced contraction in small detrusor biopsies and 2) calcium uptake and release from intracellular stores in cultured human detrusor smooth muscle cells. (HDSMC).

Methods

Detrusor biopsies were obtained from patients with benign bladder diseases undergoing cystoscopy. HDSMC were isolated and kept in culture using explant technique. Calcium was measured in single HDSMC using the calcium sensitive fluorescent probe fura-2 and fluorescence video microscopy and in monolayer using dual wavelength microfluorometry. Using a stereomicroscope mucosa free detrusor strips (3±1 mg) were mounted in 1 ml water bath containing Tyrodes buffer heated to and maintained at 37^{O}C. The muscle strip was anchored between two stainless steel pins, one of which was connected to a force transducer. Isometric force was continuously recorded. The tissue was continuously gassed with 95% O_2 and 5% CO_2 (pH 7.4). At the beginning of each protocol the responsiveness of each strip to 40 mM K^+ was recorded. The resting tension of the preparation during the equilibration period was kept at 3-4 mN throughout the experiment.

Results

DMSO (1-10%) induced a dose-dependent increase in cytosolic free calcium, ($[Ca^{2+}]_I$). The calcium rise persisted in the absence of extracellular calcium. To test the effect of DMSO on contractile force small human detrusor muscle biopsies were used. Tension was elicited by superfusing muscle biopsies with 40 mM high potassium solution. This treatment caused a rapid increase in resting tension which was followed by slow and gradual decline to resting levels. Tension development was primarily induced Ca^{2+} influx via voltage dependent Ca^{2+} channels since tension build up was not seen in Ca^{2+} free medium. Addition of 5-10% DMSO to the bathing solution quickly relaxed K+-induced muscle contraction to levels lower than pre-potassium level in the continuous presence of potassium. When the sequence was reversed, i.e, addition of DMSO 10 min prior to high potassium or tetramethyl-ammonium chloride (TEA), the solvent inhibited completely potassium and TEA induced increase in force. DMSO induced detrusor muscle relaxation could be inhibited by of potassium channels toxins.

Conclusions

In the present study, DMSO-induced relaxation of high potassium induced contraction of isolated human detrusor biopsies is demonstrated. The degree of relaxation induced by DMSO was concentration dependent. In the presence of DMSO the effect of potassium and TEA was completely antagonized. Repolarization of the tissue induced by DMSO could be blocked by potassium channels toxins. This study support the hypothesis that DMSO-induced relaxation could possibly result from activation of calcium activated potassium channels. The symptomatic relief in patients with IC induced by DMSO may partly work via relaxation of the urinary bladder.