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Yoshida A[1], Nomoto Y[1], Ikeda S [1], Horinouchi K[1], Kamikawa Y[1], Ohwatashi A[1], Kawahira K[1], Tanaka N[1]

1. Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Kagoshima University

EFFECTS OF MENTHOL ON ISOLATED DETRUSOR SMOOTH MUSCLE AND ON THE MICTURITION REFLEX IN RATS

Hypothesis / aims of study

Menthol is known to facilitate the bladder cooling reflex both in the cat and the human [1]. Recent study revealed that cold- and menthol-sensitive receptor named CMR1 or TRPM8 is expressed in a small population of dorsal root ganglion cells and activates Ca^{2+}-permeable channel. On the other hand, menthol has been showed to relax isolated gastrointestinal and bronchial smooth muscle [2]. However, the effects of menthol on isolated detrusor smooth muscle and on the micturition reflex are unclear. The aim of this study was to investigate the effects of menthol on isolated detrusor smooth muscle and on the micturition reflex in rats.

Study design, materials and methods

Female Sprague-Dawley rats (220-260 g) were used. *In vitro* : Detrusor strips (10×2mm) were placed in 10ml organ baths containing Krebs-Ringer solution, which was gassed with 95% O_2 and 5% CO_2. Approximately 1g of resting tension was applied and was kept constant by re-adjustment during the equilibration period. Mechanical responses were recorded by means of an isometric transducer. After 1 h equilibration period, acethylcholine (ACh) (10^{-6}M) or α,β-methylene ATP (10^{-6}M) was applied 15 min intervals. Each application was followed by the extensive washing. After a stabilization of contraction induced by ACh or α,β-methylene ATP, menthol (10^{-4}M, 3×10^{-4}M and 10^{-3}M) was applied to the strips 10min before the application of ACh or α,β-methylene ATP. In order to investigate relaxant responses, strips were contracted with 40mM KCl. After the contraction induced by KCl reached plateau, menthol (10^{-5}M – 10^{-3}M) was applied cumulatively. *In vivo* : Rats were anesthetized with sodium pentobarbital (40mg/kg ip). A polyethylene catheter (PE-50) was implanted into the bladder. 2 days after the operation, rats were placed in the Ballman cage without any anesthesia. Cystmetry was performed by infusion room-temperature saline into the bladder at a rate of 0.1ml/min. Micturition volumes and voiding pressure were recorded continuously before and after intravesical administration of menthol at 10^{-3}M for 30 min.

Results

In vitro : Menthol (10^{-4}M, 3×10^{-4}M and 10^{-3}M) caused a concentration dependent inhibition of the contractions induced by ACh and α,β-methylene ATP (Table). Menthol at 10^{-3}M suppressed the spontaneous contractile activity. Menthol (10^{-5}M – 10^{-3}M) caused a concentration-dependent relaxation of the strips contracted with 40mM KCl (96.86±2.42% relaxation of 40mM KCl at 10^{-3}M, n=4).

In vivo : Intravesical administration of menthol at 10^{-3}M induced no significant changes on cystometric parameters (n=4).

Table : Effects of menthol on the contractions induced by ACh (10^{-6}M) and α,β-methylene ATP(10^{-6}M).

Concentration of menthol	% inhibition of ACh-induced contraction	% inhibition of α,β-methylene ATP-induced contraction
10^{-4}M	13.72±1.66% (n=4)	21.54±3.83% (n=4)
3×10^{-4}M	19.80±4.09% (n=4)	41.54±2.59% (n=4)
10^{-3}M	93.99±0.36% (n=4)	93.88±1.11% (n=4)

Interpretation of results

Menthol inhibited the contractions induced by ACh and α,β-methylene ATP and relaxed KCl preconstricted preparation in a dose dependent manner. Menthol at highest dose suppressed the spontaneous contractile activity. These data indicate that menthol has inhibitory effects on isolated rat detrusor smooth muscle. However, intravesical administration of menthol did not affect the cystmetic parameters. This result suggests that menthol administered intravesically cannot permeate into the muscle layer of the urinary bladder in the normal rats.

Concluding message

Menthol has relaxant effect on isolated rat detrusor smooth muscle and intravesical administration of menthol has no effect on micturition reflex in normal conscious rats.

References

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