

PROPIVERINE SUPPRESS ATP-INDUCED BLADDER OVERACTIVITY THROUGH OTHER THAN ANTIMUSCARINIC MECHANISMS

Hypothesis / aims of study

We reported that oxybutynin suppress ATP-induced bladder overactivity through other than antimuscarinic mechanisms. Propiverine is known to have combined antimuscarinic and calcium antagonistic actions. We investigated the effects of propiverine on bladder overactivity induced by intravesical instillation of ATP to determine if propiverine suppress ATP-induced bladder overactivity through antimuscarinic mechanisms.

Study design, materials and methods

Under urethane anesthesia(1.2gm./kg.) cystometry(at rate of 0.04ml/min) was performed in female Sprague-Dawley rats (body weight 250 gm., 8 rats for each group). After 2 hour baseline period, protamine sulfate(10mg/ml) was instilled for 1 hour, then ATP(60mM, pH 6.0) was instilled intravesically. Propiverine, pyridoxal-5-phosphate-6-azophenyl-2',4'-disulfonic acid(PPADS, P2X receptor antagonists), 4-diphenylacetoxy-N-methylpiperidine methobromide(4-DAMP, M3 muscarinic receptor antagonists), methoctramine(M2 muscarinic receptor antagonists) were given intravenously when ATP-induced bladder overactivity is stable.

Results

When protamine sulfate was infused intravesically, intercontraction interval(ICI) was decreased to 72.9% and intravesical instillation of ATP after protamine sulfate treatment further decreased ICI to 30.2% compared to baseline(ICI in seconds; baseline 812.3 ± 81.1, protamine 592.3 ± 59.4, ATP 245.1 ± 44.0). PPADS reversed the ATP-induced ICI reduction (ICI in seconds; ATP 175.1 ± 28.0, 0.1 mg/kg 211.1 ± 33.9, 1 mg/kg 296.1 ± 43.0, 10 mg/kg 413.4 ± 63.8). Propiverine reversed the ATP-induced ICI reduction (ICI in seconds; ATP 245.1 ± 44.0, 1 µg/kg 319.5 ± 43.1, 3 µg/kg 390.0 ± 59.1, 10 µg/kg 462.4 ± 104.7). In contrast ATP-induced ICI reduction was not reversed by 4-DAMP(ICI in seconds; ATP 202.9 ± 44.4, 0.1 µg/kg 227.3 ± 62.1, 0.3 µg/kg 210.6 ± 61.0, 1.0 µg/kg 171.0 ± 28.1) and methoctramine(ICI in seconds; ATP 342.0 ± 88.8, 0.03 µg/kg 305.1 ± 98.7, 0.1 µg/kg 318.4 ± 62.1, 0.3 µg/kg 361.5 ± 103.7).

Interpretation of results

Bladder overactivity induced by intravesical instillation of ATP with protamine pretreatment was suppressed by PPADS and by propiverine, not by 4-DAMP and methoctramine.

Concluding message

Propiverine suppress ATP-induced bladder overactivity through other than antimuscarinic mechanisms.

References

<http://www.abstractsonline.com/viewer/viewAbstract.asp?CKey={C422258D-F4AF-4940-99F3-7B55EBD1C125}&MKey={B0AB6A33-1721-48D6-BF84-19E1A3C755E2}&AKey={0CEBCA69-DE5E-4928-AF08-EF9CC2A12366}&SKey={7165A289-B1AB-42D1-9FEE-3BDA1A9EB89F}>

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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	The Hanyang University institutional Animal Care and Use Committee