531

Grosse J[1], Braasch F[1], Block S[1], Heidenreich A[1], Schnizler K[1]
1. *University RWTH Aachen*

POTENCY OF INTRAVESICAL ANTIMUSCARINICS IN ATTENUATING DETRUSOR CONTRACTILITY IN A MODEL OF ISOLATED WHOLE PIG BLADDER

Hypothesis / aims of study

Intravesical application of antimuscarinics is an alternative to oral therapy of the overactive bladder (OAB). Using the model of the isolated pig bladder, we identified intravesical concentrations of clinically relevant antimuscarinic drugs that attenuate detrusor contractions.

Study design, materials and methods

Pig bladders from the local abattoir were suspended in an organ bath (37^{o}C) with carbogen-gassed Krebs solution , filled with 50 ml artificial urine (AU) and connected to a transurethral pressure transducer to record pressure amplitudes. Bladders were stimulated extravesically with acetycholine in intervals of 60 min and the Krebs solution was replaced after recording of each pressure transient (Δp). Antimuscarinic drugs were instilled by replacing 50 ml of artificial urine by 50 ml of the respective stock concentration to yield the desired intravesical concentration.

Results

The natural agonist acetylcholine is as potent as carbachol in stimulating detrusor contractions: EC_50 (acetylcholine) = 7.2 ± 1.3 µM (n=7, Mean ± SEM), EC_50 (carbachol) = 2.4 ± 1.3 µM (n=6). To avoid desensitization of the detrusor at higher agonist concentrations, pressure amplitudes are normalized to preceeding applications of 100 µM acetylcholine in all further experiments. Cumulative dose-response of acetylcholine can be recorded every 1 h reproducibly log (EC_50ref) = -4.595 ± 0.1644, n=8. Intravesical application of antimuscarinic drugs for 2 h reduces the effect of acetylcholine by shifting its EC_50ref to higher values: 25 µg/ml trospium chloride, log (EC_50ref) = -3.507 ± 0.1660, n=8; 25 µg/ml oxybutynine, log (EC_50ref) = -3.67 ± 0.1918, n=6; 200 µg/ml propiverine, log (EC_50ref) = -4.023 ± 0.2590, n=8; 25 µg/ml atropine, log (EC_50ref) = -3.472 ± 0.1859, n=6; 25 µg/ml oxyphenonium-bromide, log (EC_50ref) = -3.457 ± 0.1949, n=4.

Interpretation of results

Clinically relevant antimuscarinics in OAB therapy attenuate acetylcholine induced detrusor contractions to a different degree when applied intravesically. Using the model of the isolated pig bladder , the inhibitory effect of different concentrations of intravesical antimuscarinics can be monitored for several hours. Because of the desensitization of the detrusor muscle, our model of whole isolated pig bladder does not allow to differentiate if the effects of acetylcholine will be antagonized in a competitive or none-competitive fashion.

Concluding message

Given the large availability of domestic pib bladders, this model may help to work out effective concentrations when optimizing intravesical treatment by developing a drug-delivery system for OAB prior to in vivo studies.

Specify source of funding or grant	**Funded by the Federal Ministry of Education and Research (BMBF), Germany; Grant No. 01EZ0913**
Is this a clinical trial?	**No**
What were the subjects in the study?	**NONE**