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A1-BLOCKER COADMINISTERED WITH ANTIMUSCARINIC DRUG COMPENSATES FOR THE EMPTYING DYSFUNCTION OF THE DETRUSOR MUSCLE

Hypothesis / aims of study

Detrusor overactivity (DO) coexists with bladder outlet obstruction (BOO). α_1-adrenoceptors (α_1-ARs) blockers are mainly used to treat voiding and/or storage symptoms suggestive of BOO and DO. However, α_1-blockers primarily targeting the prostate may not always alleviate storage symptoms in the bladder. Many recent clinical studies indicate the usefulness to combine α_1-AR blocker and an antimuscarinic agent. In the present study we investigate the use of α_1-blocker and an antimuscarinic agent on a rat model with DO .

Study design, materials and methods

Female Sprague-Dawley rats were used in this study. Control cystometrography (CMG) was followed by left middle cerebral artery occlusion (MCAO). Rats were divided into 4 drug administration groups: 1) tamsulosin intravenous (iv) administration (TAM: 10^{-1}-10^{3} μg/kg), 2) solifenacin iv administration (SOL: 10^{-2}-1.0 mg/kg), 3) solifenacin iv administration (10^{-1}, 3 x 10^{-1}, 1.0 mg/kg) with 1-hour intervals during continuous iv administration of TAM (10^{-2} μg/kg/5 hours), 4) combined iv administration of TAM (10^{-2}, 10^{-1} μg/kg) and SOL (10^{-2} mg/kg).

Results

Bladder capacity (BC) was markedly reduced after middle cerebral artery occlusion and remained consistently lower than 50% of the preocclusion volume. Both TAM and SOL alone significantly increased BC in a dose-dependent manner. There were no significant differences in percentage increase in BC between mono-administration of SOL (group 2) and continuous combined administration (group 3). However, combined administration (group 4) with TAM (10^{-1} μg/kg) and SOL (10^{-2} mg/kg) significantly increased BC by 68.8% of control, when compared to mono-administration of 10^{-2} mg/kg SOL (19.8%). No significant difference was found in bladder contraction pressure between groups 2 and 3. SOL dose-dependently decreased bladder contraction duration (BCD) and a significant reduction (by 35.0% of control) was found at the high dose (1.0 mg/kg). In group 3, however, no reduction was found even at the high dose (1.0 mg/kg) of SOL. TAM prevented the reduction in BCD induced by the administration of high-dose SOL.

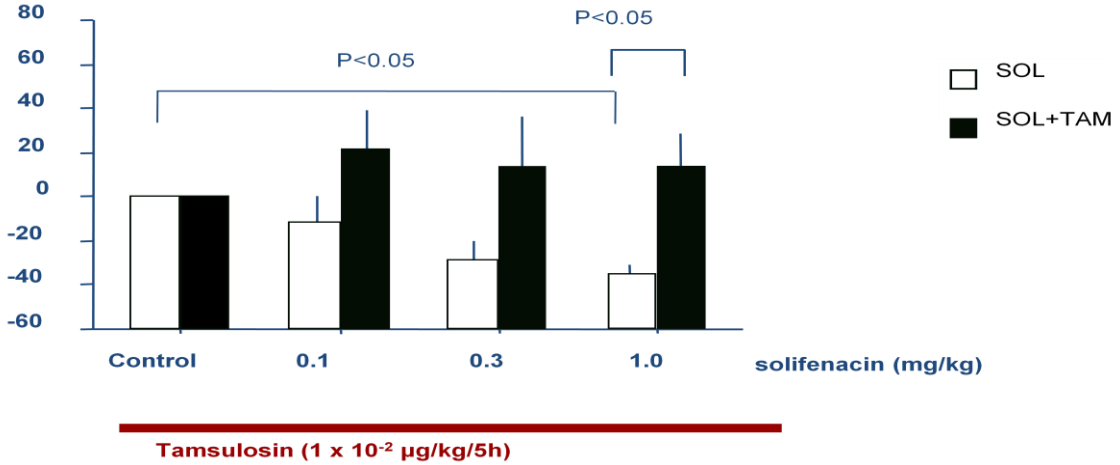

Figure: Effect of compounds on the bladder contraction duration. SOL dose-dependently decreased bladder contraction duration. In rats with combined administration, no reduction was found even at the high dose (1.0mg/kg) of SOL.

Interpretation of results

These results suggest that combination treatment with α_1-AR blocker and an antimuscarinic drug have an additive effect on DO at low doses. Furthermore, the study indicates the α_1-AR blocker TAM might have some action in the urethra to compensate for the emptying dysfunction of the detrusor when an antimuscarinic drug is co-administered.

Concluding message

Combination treatment with α-AR blocker and antimuscarinic drug is believed to be useful not only for enlargement of the bladder but also compensation for emptying dysfunction.

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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	**University of Fukui**