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INHIBITORY EFFECT OF L-TYPE VOLTAGE DEPENDENT CALCIUM CHANNEL (VDCC) BLOCKER AND ETHANOL ON THE URINARY BLADDER CONTRACTION OF RAT

Hypothesis / aims of study

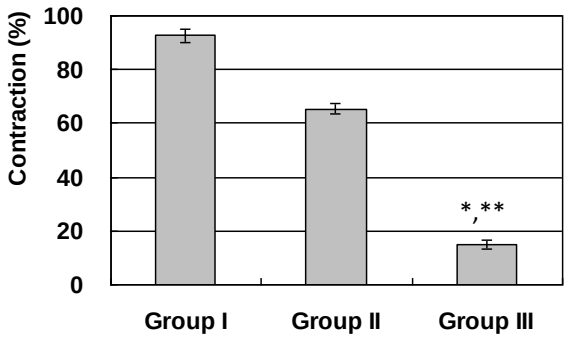
Acute ethanol intoxication is one of the risk factors for acute urinary retention. In animal studies, ethanol significantly impaired detrusor contractability *in-vivo* and *in-vitro* [1]. The exact mechanisms of ethanol-induced acute urinary retention have not been elucidated yet. Recently ethanol is known to have direct suppressive effect on L-type VDCC in various organ studies. This study was performed to assess the effect of L-type VDCC blocker (dilitiazem) on the response of the urinary bladder with ethanol intoxication in *in-vivo* and *in-vitro* studies.

Study design, materials and methods

Sprague-Dawley rats were used for *in-vivo* and *in-vitro* studies. For *in-vitro* study, bladder smooth muscle strips were prepared. After achieving isometric tension by carbachol (100 uM), the tension changes was monitored. The strips were divided into 3 groups according to pretreatment. Group I was pretreated with ethanol (0.5%), group II with diltiazem and group III with diltiazem followed by ethanol. After each pretreatment, the carbachol (100 uM) induced tension changes of the bladder strip were monitored. The carbachol induced tension was compared before and after each pretreatment. In separate *in-vivo* experiments (filling cystometry), the changes of maximal voiding pressure (MVP) and intercontractions interval (ICI) after intra arterial administration of each agents (identical grouping with *in vitro* study) were monitored.

Results

Figure showed the result of *in-vitro* strip study. The carbachol induced tension increment in group I, group II and group III was significantly decreased after each pretreatment (92.6±2.5%, 65.4±2.0%, 14.9±1.4% of the control, respectively). The degree of the tension decrement was significantly greater in group III than in group I or II.



Group I; Ethanol intoxication (0.5%)
Group II; Diltiazem pretreatment (1X 10^{-6}M)
Group III; Diltiazem pre-treatment followed by ethanol intoxication
*; significantly different from group I
**; significantly different from group II

Table showed the result of *in-vivo* study. The MVP was not decreased after ethanol (0.5%) (p=0.080), but was significantly decreased (p=0.000) after diltiazem or diltiazem/ethanol. The inter-contraction interval (ICI) was significantly prolonged in all three different experimental group. The degree of the decrement of MVP or prolongation of ICS was numerically greater in group III than in group I or II.

In vivo	MVP (cmH2O)				ICI (sec)			
	Before	**After**	**Δ (%)**	**P-value**	**Before**	**After**	**Δ (%)**	**P-value**
Group I	23.4	14.9	-38.7	0.000	116.9	154.4	36.3	0.000
Group II	26.5	24.4	-9.6	0.080	118.4	153.6	24.0	0.001
Group III	26.2	10.0	-50.5[*,**]	0.000	116.2	174.2	56.5[*,**]	0.003

*; significantly different from group I
**; significantly different from group II

Interpretation of results

From the *in-vitro* and *in-vivo* study, diltiazem and ethanol synergistically inhibited the carbachol induced detrusor contraction. By these results, it is conceived that ethanol and L-type VDCC blocker seem to inhibit detrusor contraction via common pathway.

Concluding message

Due to the inhibitory effect of ethanol on L-type VDCC, the risk of acute urinary retention with acute ethanol intoxication might increase in patients with diltiazem medication.

References

1. BJU Int (1999) 83:686-92.

Specify source of funding or grant	**none**
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	**Care and Use of Laboratory Animals from Korea Food & Drug Administration**