MP38-7 The effect of beta-3 adrenergic receptor agonist on micromotions of major pelvic ganglion disconnected rat bladder

*Hee Seo Son, Soo Young Moon, Hyun Kyu Ahn, Kyung Taek Oh, Jee Soo Park, Jee Soo Ha, and Jang Hwan Kim**

From the Department of Urology and Urological Science Institute, Yonsei University College of Medicine, Seoul, Korea

Background

◆ **What is Micromotion**
Micromotion is intrinsic localized motility of bladder wall, comprising microcontractions and microelongations

◆ **How is Micromotion generated**
Micromotion is regarded to be associated with disinhibited autonomy expressed when normal descending inhibitory influences are lost

◆ **Can we detect micromotion with CMG**
Increased coordination of micromotion waves may be expressed as intravesical phasic pressure fluctuations in case of altered neural modulation

◆ **Why is micromotion important**
Local distortion of bladder wall made by autonomous micromotions may generate afferent nerve activity resulting in increased filling sensation, urgency, or pelvic pain

◆ **Can we modulate micromotion**
β3-adrenoceptor agonists showed effectiveness in inhibiting mechanosensitive bladder afferent activity, which may be related to suppression of bladder microcontractions

◆ **Subjects to be elucidated for clinical application**
For effective management of patients with defect in neural pathway, proper therapeutic target should be defined, and the followings are to be clarified

✓ The site responsible for initiation and/or propagation of micromotions
✓ The effect of β3-adrenoceptor agonists on micromotion in living animal
✓ The action site of β3-adrenoceptor agonists

References

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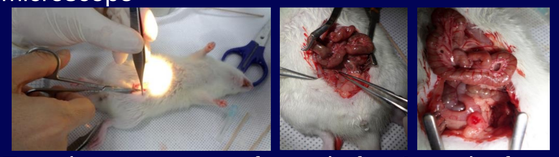
Objectives

To evaluate the effect of beta-3 adrenergic receptor agonist on micromotions of major pelvic ganglion disconnected rat bladder

Methods

◆ **Animals**
Male Sprague-Dawley rats (N=18)

◆ **Disconnection of major pelvic ganglion**
Rats were anesthetized with 2% isoflurane in oxygen. MPGs were identified in the lateral aspect of the prostate and were carefully removed under microscope



Experiments were performed after 1 week of adaptation period following MPG disconnection

◆ **Groupping of subject animals**
1. β3 adrenergic receptor agonist (CL-316243) group
2. β3 adrenergic receptor antagonist (SR59230A) pretreated CL-316243 group
3. Non-selective muscarinic receptor antagonist (Oxybutynin) group

◆ **Cystometogram**
PE-50 tubing was introduced into in the bladder and cystometry was performed by infusing physiological saline at a rate of 0.12ml/min

◆ **Assessment**
Frequency of micromotion was checked at baseline, after administration of vehicle (saline) (i.a.), after administration of each target agent (i.a.) consecutively

Results

◆ Micromotion frequency was significantly decreased after injection of CL-316243 (2.2±3.5/10min) compared to baseline (7.5±2.6/10min) (P=0.005)
◆ There was no significant change of micromotion frequency in SR59230A pretreated CL-316243 group (6.3±2.9/10min) compared to baseline (6.3±0.5/10min) (P=1.000)
◆ The number of micromotion after Oxybutynin injection (3.2±3.1/10min) was not significantly different from that of baseline (5.7±3.1/10min) (P=0.059)

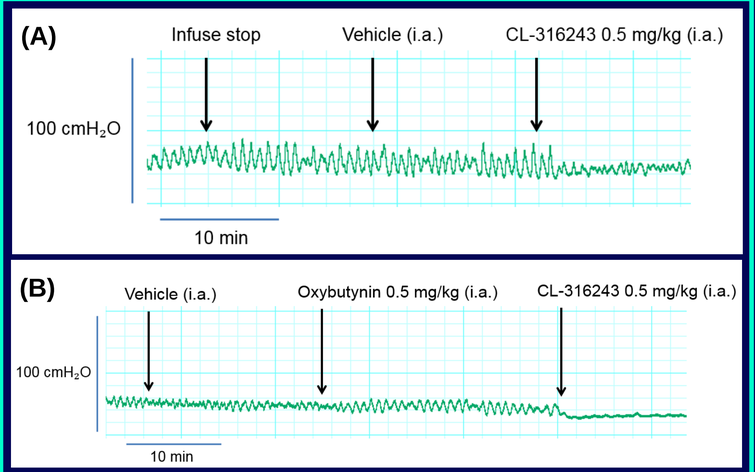


Figure1. Representative recording of micromotion, (A) The frequency of micromotion was significantly decreased after intra-arterial administration of beta-3 adrenergic receptor agonist (CL-316243) (0.5mg/kg), (B) The frequency of micromotion was not significantly decreased after intra-arterial administration of Oxybutynin (0.5mg/kg). However after administration of the beta-3 adrenergic receptor agonist (CL-316243) (0.5mg/kg), noticeable decrease in frequency of micromotion was observed

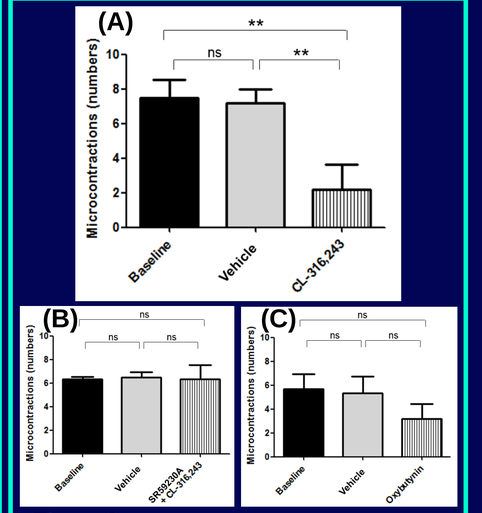


Figure2. Frequency change of micromotion of each group (mean number per 10 minutes) (A) CL-316243 group (n=6) (B) SR59230A pretreated CL-316243 group (n=6), (C) Oxybutynin group (n=6); ** , significant at P<0.01

Conclusions

◆ We could observe that systemically administrated beta-3 adrenergic receptor agonist have effect in alleviating micromotions of MPG disconnected rat bladder
◆ These results also suggest that beta-3 adrenergic receptor agonist might be an effective agent in controlling the initiation of overactive bladder