312

Cheng C L[1], Peng C W[2], Chen J J[2], Huang S C[1], Chang H Y[3], de Groat W C[3]
1. Div. Urology, Dept. of Surgery, Taichung Veterans General Hospital, Taiwan, R.O.C., 2. Institute of Biomedical Engineering, National Cheng Kung University, Taiwan, R.O.C., 3. Department of Pharmacology, University of Pittsburgh School of Medicine, Pennsylvania, USA

EFFECT OF 8-OHDPAT ON EXTERNAL URETHRAL SPHINCTER (EUS) ACTIVITY IN PUDENDAL NERVE INJURY RATS

Hypothesis / aims of study

Pudendal nerve injury (PNI) is an accepted animal model for studying stress urinary incontinence (SUI). Our previous studies [1,2] indicated that PNI rats exhibited voiding abnormalities including increased volume threshold for initiating voiding, increased contraction duration and residual volume, decreased leak point pressure and voiding efficiency, and changes in the pattern of EUS EMG activity. Although the serotonergic agent duloxetine has been used clinically in treatment of SUI patients, its effects as well as the effects of other serotonergic drugs on EUS activity have still not been fully investigated. This study used cystometry and EUS electromyography to examine the effects of serotonergic agonist drug, 8-hydroxy-2-(di-n-propylamino)tetralin (8-OHDPAT), on cystometry and EUS activity in female urethane-anesthetized rats following chronic bilateral pudendal nerve injury.

Study design, materials and methods

Fifteen female Sprague-Dawley rats (weighing between 300 and 350 g) were used in these experiments. The rats received bilateral pudendal nerve transections. After 6 weeks of recovery, cystometrography (CMG) and EUS electromyography (EUS EMG) were performed before or after administration of 8-OHDPAT (0.2 mg/kg, i.v.).

Results

All animals before administration of any drugs exhibited micturition reflexes during CMGs. After administering 8-OHDPAT, PNI rats exhibited increased contraction duration (1-2 fold increase), voided volume and voiding efficiency, decreased volume threshold (10%-15%) for initiating voiding, decreased residual volume (40%-50%) and decreased bladder contraction amplitude (20-30%). The EUS activity appeared as clusters of prominent bursting contractions immediately after drug administration and throughout the entire storage phase. EUS EMG during the voiding phase, showed a significant increase in silent period and bursting period, and decrease in bursting frequency.

Interpretation of results

Our results indicate that the pudendal nerve is not essentially for reflex micturition so that all of animals voided during continuous bladder infusion. PNI rats exhibited voiding abnormalities, which might be partially attributed to loss of both the sensory and motor branches of the pudendal nerve.

8-OHDPAT significantly increased voided volume, decreased residual volume, and improved voiding efficiency. Previous studies indicated EUS bursting activity during micturition could promote the release of urine. In our experiment, 8-OHDPAT significantly enhanced the EUS pumping activity, including both an increase in the silent period and reduced bursting frequency. Hence the drug had a significant effect on the EUS even after injury to the pudendal nerve.

Concluding message

These results indicate that 8-OHDPAT changed the pattern of EUS activity and significantly improved voiding function in pudendal nerve injured rats.

References

[1] External Urethral Sphincter Activity in a Rat Model of Pudendal Nerve Injury, Neurourology Urodynamics, 2006
[2] Effect of acute pudendal nerve injury on external urethral sphincter (EUS) activity in the rat, the 35th annual meeting of the society for neuroscience, Washington, USA, 2005

FUNDING: This study was supported by grants from the National Science Council, Taiwan, R.O.C. (NSC94-2214-B-075A-019), and Industrial Technology Research Institute grants in Taiwan to CL Cheng.
DISCLOSURES: NONE
ANIMAL SUBJECTS: This study followed the guidelines for care and use of laboratory animals and was approved by Institutional Animal Care and Use Committee of Taichung Veterans General Hospital, Taiwan