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IMPROVING VOIDING EFFICIENCY IN THE DIABETIC RAT BY A 5-HT1A SEROTONIN RECEPTOR AGONIST

Hypothesis / aims of study

Serotonin affects micturition in the normal rat through actions not only on ascending and descending spinal pathways and supraspinal centers but also on the lumbosacral spinal cord level. The selective 5-HT1A receptor agonist, 8-OH-DPAT, reversed detrusor-sphincter dyssynergia (DSD) in the spinal cord injury (SCI) rat, thereby improving voiding efficiency. Rats with experimental diabetes mellitus (DM) have been shown to have both bladder and urethral dysfunction during reflex voiding. We therefore examined the effects of 8-OH-DPAT on micturition in DM rats.

Study design, materials and methods

Female SD rats weighing 250-275 g were used. DM was induced by an intraperitoneal injection of streptozotocin (65 mg/kg) and a cystometric study was performed 8 weeks post-injection. Intravesical pressure was monitored in urethane-anesthetized animals via a transvesical catheter. External urethral sphincter electromyography (EUS-EMG) was also measured. The 5-HT1A antagonist WAY-100635 was administered after each 8-OH-DPAT dose-response curve (all drugs were administered intravenously, iv).

Results

Compared to controls, DM rats had a higher bladder capacity, micturition volume and residual volume, and a lower peak bladder pressure and voiding efficiency. In DM rats, 8-OH-DPAT (3-1000 ug/kg, iv) induced significant dose-dependent increases in micturition volume, significant dose-dependent decreases in residual volume, resulting in significant increases in voiding efficiency. There was a dose-dependent increased phasic EUS activity and a relative increase in EUS “open time” during the micturition event. This was correlated with the improved voiding efficiency. WAY-100635 (300 ug/kg, iv) partially or completely reversed all 8-OH-DPAT-induced changes.

Interpretation of results

Both the bladder voiding efficiency and the periodic EUS activity were decreased in DM rats. 5-HT1A receptor agonism increased micturition volume, decreased residual volume, and promoted periodic EUS activity, thereby improving voiding efficiency.

Concluding message

5-HT1A serotonin receptor agonist, 8-OH-DPAT improved the voiding efficiency in the diabetic rat. Whether or not these results may have implications for the future treatment of voiding dysfunction in DM patients remains to be studied.

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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	**The animal care and use committee of Shanghai Sixth People’s Hospital, in line with internationally known guidelines.**