

IMPROVING VOIDING EFFICIENCY BY THE 5-HT_{2A/2C} RECEPTOR AGONIST, DOI, ON MICTURITION IN THE DIABETIC RAT

Hypothesis / aims of study

Both the bladder voiding efficiency and the periodic EUS activity were decreased in DM rats. 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. In a previous study we showed that the selective 5-HT_{1A} receptor agonist, 8-OH-DPAT, increased micturition volume, decreased residual volume, and promoted periodic EUS activity, thereby improving voiding efficiency. 5-HT_{2A} receptors are also found both in the dorsal horn and in the lumbar dorsolateral nucleus (Onuf's nucleus) driving the EUS and external anal sphincter. We therefore examined the effects of the 5-HT_{2A/2C} receptor agonist, DOI, 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 6 weeks post-injection. Intravesical pressure was monitored in urethane-anesthetized animals via a transvesical catheter. External urethral sphincter (EUS)-generated high frequency oscillations (HFOs) of intravesical pressure were assessed. The 5-HT_{2A} receptor antagonist ketanserin was administered after each DOI 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, DOI (0.01-0.3 mg/kg. iv) induced a significant dose-dependent increase in micturition volume and significant dose-dependent decreases in residual volume and bladder capacity. There was also a dose-dependent increase of the high-frequency oscillation (HFO) activity, evident as an increase in the number of small oscillations per voiding. Ketanserin (0.1 mg/kg. iv) partially or completely reversed all DOI-induced changes.

Interpretation of results

In DM rats, DOI induced a dose-dependent increase of the high-frequency oscillation (HFO) activity, evident as an increase in the number of small oscillations per voiding. This was correlated with a improving of the phasic EUS activity and a relative increase in EUS "open time" during the micturition event, resulting in the improved voiding efficiency. .

Concluding message

Taken together, these data suggest that both the bladder voiding contraction and the external urethral sphincter (EUS)-generated high frequency oscillations (HFOs) of intravesical pressure are decreased in DM rats. The 5-HT_{2A/2C} receptor agonist, DOI, improves the bladder voiding contraction, and promotes the HFOs activity, thereby improving voiding efficiency. Whether or not these results may have implications for the future treatment of voiding dysfunction in DM patients remains to be studied.

References

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Disclosures

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