Tadalafil improves urethral function in diabetic rats

Gotoh D1, Torimoto K1, Miyake M1, Morizawa Y1, Hori S1, Onishi K1, Iida K1, Yamada A1, Nakai Y1, Fujimoto K1
1. Nara Medical University

**Background**
In ICS 2016, we showed that tadalafil improves the bladder’s blood supply and lower urinary tract dysfunction in diabetic rats. At that time we evaluated lower urinary tract function by cystometry and mainly looked at bladder function. The result suggested that tadalafil may improve urethral function during micturition. Therefore, we directly measured urethral pressure and investigated the effect of tadalafil on urethral dysfunction in diabetic rats.

**Materials and methods**
- Female Sprague-Dawley rats
- Diabetes induction: Streptozotocin 65 mg/kg i.p.
- Three groups: Non-diabetes (ND) Diabetes (D) Diabetes with tadalafil (DT)
- Urethral perfusion pressure (UPP) 7 weeks after diabetes induction
- Tadalafil was orally administrated at 2mg/kg/day for 7 days before the experiment.

**Results**

**Baseline UP**
- ND group: 20.5 ± 5.2 cmH2O
- D group: 23.8 ± 4.9 cmH2O
- DT group: 20.0 ± 4.5 cmH2O

**UP nadir**
- ND group: 16.5 ± 3.8 cmH2O
- D group: 18.0 ± 4.2 cmH2O
- DT group: 15.0 ± 3.2 cmH2O

**IPUR**
- ND group: 35.0 ± 6.2 cmH2O
- D group: 30.0 ± 5.4 cmH2O
- DT group: 20.0 ± 4.5 cmH2O

**UP reduction**
- ND group: 15.0 ± 3.8 cmH2O
- D group: 18.0 ± 4.2 cmH2O
- DT group: 10.0 ± 3.2 cmH2O

**Amplitude of HFO**
- ND group: 2.0 ± 0.5 cmH2O
- D group: 4.0 ± 1.0 cmH2O
- DT group: 6.0 ± 1.5 cmH2O

IPUR was significantly lower in the DT group than in the D group (18.9 ± 2.9 vs. 29.1 ± 6.6 cmH2O, p<0.05)

**Interpretation of results**
Urethral relaxation function during micturition was impaired in diabetic rats. This result is consistent with those of our previous study1) in which we used the same model of diabetes and a different method of measuring urethral pressure. In the same study, we demonstrated that the administration of L-arginine as an NO donor improves urethral function. Tadalafil inhibits PDE5, increases cyclic GMP in smooth muscle, and induces their relaxation of smooth muscle. As a result, tadalafil acts as an NO donor. The administration of tadalafil induced the appropriate start of micturition (opening urethra) and efficient urine flow.


**Conclusion**
Tadalafil improves urethral function during micturition by acting as an NO donor in diabetic rats.

There is no conflict of interest.