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ACETYLCHOLINE RELEASES FROM URINARY BLADDER SMOOTH MUSCLES OF NON-INSULIN-DEPENDENT DIABETES RAT (GK RAT)

Aims of Study

Clinical lower urinary tract dysfunction related to diabetes is well known. Although, chronic diabetes mellitus causes the damage of autonomic nervous system and peripheral nerves, however, the exact mechanism is not clearly understood. Therefore, we attempted to measure ACh release and detrusor pressure induced by electrical field stimulation (EFS) on pelvic nerve of non-insulin-dependent diabetes rats with using in vivo microdialysis technique.

Methods

8 and 32 weeks-old female Goto-Kakizaki rats (GK rat; non-insulin-dependent diabetes mellitus model) and age-matched female wistar rats (control) were used in this study. They were anesthtized with 0.9mg/kg urethane, and the lower abdominal cavity was opened with a mid-line incision, bilateral ureters were ligated and dissected, and the pelvic nerves were sectioned bilaterally at the central end of the pelvic plexus. The peripheral end of one of the pelvic nerves was placed on a bipolar platinum electrode. Electrical field stimulation (EFS) on pelvic nurve (supramaximum voltage, pulse duration 0.1 msec, frequency 1-10 Hz, train of pulse 60s) was applied, and detrusor pressure was recorded.
To measure detrusor pressure in the urinary bladder, a 20 G cannula was transurethrally inserted into the bladder, and was connected to a pressure transducer (AP-620G; Nihon Kohden, Tokyo, Japan). The microdialysis probe (O-P-30-5, Eicom Co., Kyoto, Japan) was inserted into the bladder wall and the inlet cannula of the probe was connected to a microinfusion syringe pump (EP-60, Eicom Co.). Ringer solution with containing 100 μM physostigmine sulfate was continuously perfused at a rate of 2 μl/min. In the present experiment, sumpling was started at 10 min before stimulation and dialysate was collected in a microtube every 10 min, and a volume of 10 μl was injected into the ACh assay system. The amount of ACh in the dialysate fraction was measured by HPLC with ECD as previously reported (1). The comparison of detrusor pressure and ACh releases induced by EFS on pelvic nurve between GK rats and age-matched control wistar rats were evaluated.

Results

EFS caused frequency-dependent bimodal phasic and tonic contractions of the bladder of all rats in both groups. In 8 weeks-old rats, the maximum detrusor pressure of control rats was 27.2±6.0 cmH_2O, which was not significantly different from GK rats (36.9±6.0 cmH_2O).
In 32 weeks-old rats, the maximum detrusor pressure of GK rats was 38.7±7.0 cmH_2O, which was significantly lower than that of control rats (56.8±21.2 cmH_2O).
EFS on pelvic nurve produced frequency-dependent acetylcholine releases in both groups. In 8 weeks-old, the amount of acetylcholine release at 10Hz of control rats and GK rats were 0.82±0.07 and 0.77±0.23 pmol/injection, respectively. There were not significant difference between the values.
In 32 weeks-old rats, the amount of acetylcholine release at 10 Hz of GK rats was 0.56±0.13 pmol/injection, which was significantly lower than that of control rats (1.00±0.15 pmol/injection).

Conclusions

The present study showed that there is a significant decrease in EFS-induced ACh releases and detrusor pressure in chronic phase of GK rat, which may contribute to bladder voiding dysfunction in diabetes mellitus.
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References

1. Life Sci., 62, PL 393-399, 1998