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PREVENTIVE EFFECT OF CYCLOHEXENONIC LONG-CHAIN FATTY ALCOHOL ON RAT OVERACTIVE BLADDER INDUCED BY BLADDER NECK OBSTRUCTION

Hypothesis / aims of study

It is well known that benign prostatic hyperplasia (BPH) induces myogenic overactive bladder (OAB). However, the etiological and morphological alterations in OAB induced by BPH are still unclear. The tropical plant *Hygrophilia erecta* Hochr. has been shown to contain some cyclohexenonic long-chain fatty alcohol that has neurotrophic activities on cultured neurons from the cerebral cortex. The C26-alcohol n-hexacosanol has been found to directly increase neurite extension as well as biochemical differentiation of these neurons directly[1,2]. Thus, n-hexacosanol has an NGF-like effect on various cells and neurons. NGF is reported to play an important role in the bladder neck obstruction (BNO) rat bladder[3]. We have reported the preventive effect of long-chain fatty alcohol on diabetes-induced neuropathy and ischemia-reperfusion injury in the rat bladder[1,2]. In this study, we investigated the preventive effect of cyclohexenonic long-chain fatty alcohol on rat OAB induced by mild BNO.

Study design, materials and methods

Mild partial BNO was created by ligation of the female SD rat urethra[3]. Female SD rats (10 weeks old) were divided into three groups: those receiving mild BNO without treatment with cyclohexenonic long-chain fatty alcohol, 3-(15 hydroxypentadecyl) 2,4,4-trimethyl cyclohex 2-en 1-one (OB group), those treated with cyclohexenonic long-chain fatty alcohol (8 mg/kg, i.p, every day) (C-1 group) and the age-matched control group (CONT) (in each group, n = 6-8). Six weeks after the induction of BNO, voiding behaviors of rats were observed in the metabolic cage, and CMG was performed in the experimental animals under urethane anesthesia. Furthermore, H&E and Bodian staining were performed to calculate the ratio of smooth muscle and density of neurofibrils in these bladders. Statistical comparison of differences between the groups was performed using analysis of variance and Fisher's multiple comparison tests. $P< 0.05$ was regarded as the level of significance.

Results

Bladder weight and voiding behaviors in the experimental animals are shown in TABLE 1. Bladder weight in the OB group was significantly lager than that in the CONT group (0.15 and 0.11 g, respectively). Miction frequency in the OB group was significantly lager than] that in the CONT or C-1 groups, and one voided volume in the OB group was significantly smaller than [that in the CONT group. CMG and H&E staining and Bodian staining data are shown in TABLE 2. Maximum contraction pressure of detrusor (Pdet) in the OB group was significantly larger than in the CONT group, and one voided volume in the OB group was significantly smaller than in the CONT group. The ratio of smooth muscle in the OB bladder was significantly larger than that in the CONT or C-1 bladder (76.9, 72.4, 70.2 percent, respectively). Neurofibrils in the OB group were significantly smaller than those in the CONT or C-1 groups (2.58, 5.01, 5.62 /mm^2, respectively).

TABLE 1. Bladder weight and voiding behaviors in the experimental animals

Group	bladder weight	miction frequency/day	voided volume ml/day	one voided volume ml
CONT	0.109 ± 0.004	11.5 ± 1.5	7.9 ± 2.7	0.809 ± 0.166
OB	0.150 ± 0.010*	21.3 ± 2.5**	9.7 ± 1.7	0.421 ± 0.092*
C-1	0.138 ± 0.012*	14.7 ± 1.5	7.9 ± 1.5	0.515 ± 0.149 .

*) significantly different from CONT group. **) significantly different from CONT and C-1 groups.

TABLE 2. CMG and H&E staining and Bodian staining data in the experimental animals

Group	Pdet (cmH_2O)	one voided volume ml	% smooth muscle area	neurofibrils /mm^2
CONT	36.9 ± 2.9	0.450 ± 0.050	72.4 ± 1.2	5.01± 0.63

OB	66.4 ± 9.4*	0.276 ± 0.049*	76.9 ± 1.4**	2.58 ± 0.51**
C-1	56.2 ± 6.9*	0.447 ± 0.155	70.2 ± 2.0	5.62 ± 0.90 .

*) significantly different from CONT group. **) significantly different from CONT and C-1 groups.

Interpretation of results

In this study, we demonstrated that BNO rats in the present experiments were under OAB condition. In the condition of BNO, as functional denervation of neurofibrils is reported, little is known about morphological alterations in the bladder[3]. Our data suggest that under OAB condition, the density of neurofibrils is decreased, which is prevented by treatment with cyclohexenonic long chain fatty alcohol. As cyclohexenonic long chain fatty alcohol has a preventive effect on nerve injury and NGF-like effect, it is possible that this effect on bladder dysfunction may be caused by a preventive effect of peripheral nerve alterations in the bladder[1,2].

Concluding message

BNO induces OAB and denervation of neurofibrils in the bladder. This bladder dysfunction is prevented by treatment with cyclohexenonic long chain fatty alcohol.

References

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