208

Furuno T[1], Tanaka H[1], Kakizaki H[2], Kitta T[1], Mitsui T[1], Nonomura K[1]
1. Department of Urology, Hokkaido University Graduate School of Medicine, 2. Department of Urology, Asahikawa Medical College

CHOLINERGIC COMPONENT OF MICTURITION CONTRACTIONS INCREASE IN MICE WITH MILD BLADDER OUTLET OBSTRUCTION: CONSCIOUS CYSTOMERTIC STUDY.

Hypothesis / aims of study

Several animal models have been developed to examine the functional alterations of the bladder following bladder outlet obstruction. Development of genetic manipulation technology offered a mice model is a useful tool to investigate molecular mechanisms underlying various forms of bladder dysfunction. Previous studies using rats indicated that contribution of cholinergic mechanism to micturitoin contraction changes after bladder outlet obstruction, while this phenomenon has not been well studied in mice. In the present study, we established the mild bladder outlet obstruction model in mice and investigated the alterations in cholinergic component of micturition contractions on conscious cystometry.

Study design, materials and methods

Female C57BL/6 aged 7 weeks were used. To create partial bladder outlet obstruction, separated urethra and 27G needle were ligated with 4-0 nylon together and needle was subsequently removed (BOO group, N=8). In sham operation group (N=10), ligation was skipped. Five weeks after surgery, conscious cystometry was performed. Cystostomy catheter was inserted under isoflurene inhalation. After 1 to 2 hours of recovery time, saline at room temperature (1.5 ml/h) was infused and bladder pressure was measured. To investigate the contribution of cholinergic mechanism in micturiton contraction, atropine (0.1 and 1 mg/kg s.c.) was administrated. Cystometirc parameters including micturition pressure, micturition volume, residual volume, bladder capacity and voiding efficacy were examined.

Results

Bladder weight increased 1.8-fold in BOO (sham 23+-0.3 µg vs. BOO 43+-0.3 µg, $p<0.001$). Reproducible micturition contractions could be observed during filling cystometry in both groups before and after atropine injection (fig. 1).
On baseline cystometry, a significant difference was noted between two groups in micturition volume (88+-9 µl in BOO vs. 133+-8 µl in sham, $p<0.01$), bladder capacity (113+-9 µl in BOO vs. 143+-8 µl in sham, $p<0.05$), and residual volume (25+-2 µl in BOO vs. 11+-2 µl in sham, $p<0.001$). Voiding efficacy was also significantly different between two groups (77+-2 % in BOO vs. 93+-1 % in sham, $p<0.001$). However, there was no significant difference in micturition pressure (vs. 32.5 cmH_2O in sham, vs. BOO 31.9 cmH_2O).

In both obstructed and sham operated mice, injection of 0.1 mg/kg and 1.0 mg/kg of atropine reduced significantly micturition pressure, micturition volume and voiding efficacy. Reversely a significant increase in residual volume was found in both groups after injection of atropine (fig. 2 and 3).

When compared between two groups inhibitory effects of atropine in percent variation of voiding efficacy were more pronounced in BOO than those in sham (0.1mg/kg; sham -14+-5 % vs. BOO -39+-6 %, $p<0.01$, 1mg/kg; sham -22+-4 % vs. BOO -43+-6 %, $p<0.01$, fig. 3). In addition, inhibitory effect of 0.1mg/kg atropine on voiding efficacy was more promoted to the same level after 1mg/kg atropine only in BOO (fig. 3).

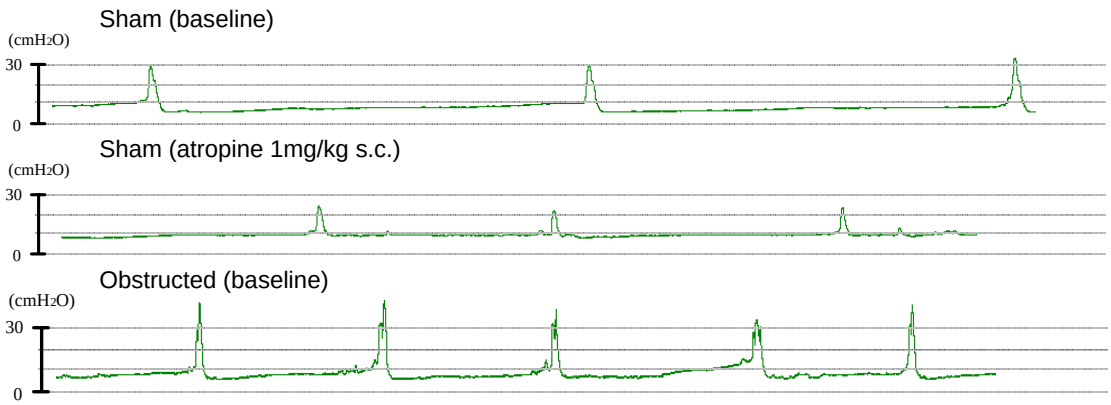
Interpretation of results

In the present study, bladder outlet obstruction induced a limited increase in bladder weight, and micturition pressure was not significantly different between two groups. These results reflected that the degree of obstruction in this model was relatively mild. Otherwise increasing residual volume, and decreasing micturition volume and voiding efficacy are comparable to those seen in men with benign prostate hyperplasia (BPH). The inhibitory effects of atropine on micturition reflex were similar in obstructed and sham-operated mice, but its effect on voiding efficacy was more promoted in mild obstructed mice.

Concluding message

The present bladder outlet obstruction model in mice is valuable to investigate underlying mechanism of bladder dysfunction in human BPH. Since an inhibitory effect of atropine on voiding efficacy is pronounced, cholinergic contribution to micturition contractions is alliterated by bladder outlet obstruction in mice. These results suggest that increase of cholinergic component is a part of compensating mechanism to bladder outlet obstruction.

Figure 1: Representative records of cystometery before and after administration of atropine.



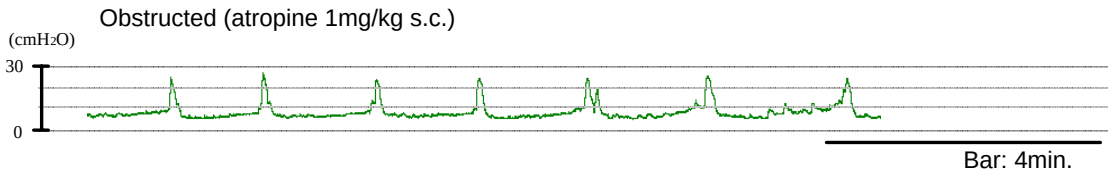


Figure 2: After atropine administration, micturition pressure and micturition volume decreased, and residual volume increased dose-dependently in sham and BOO.

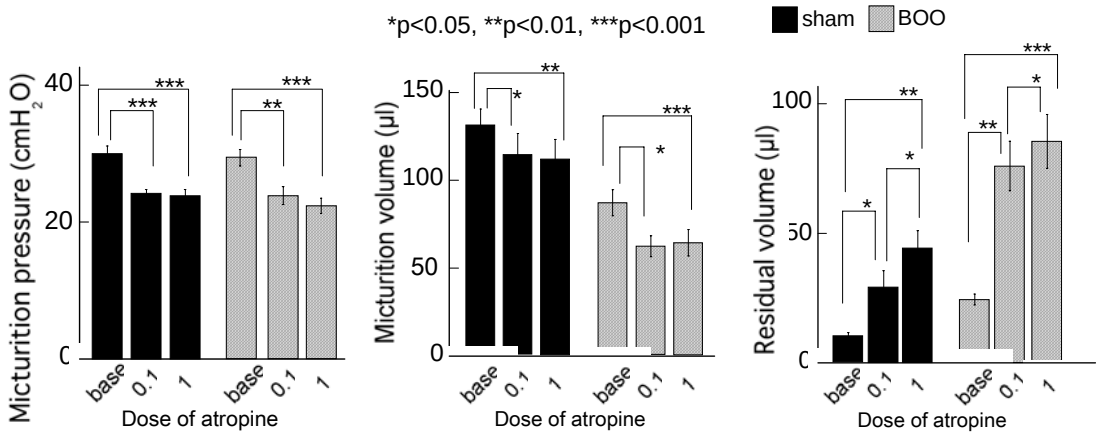
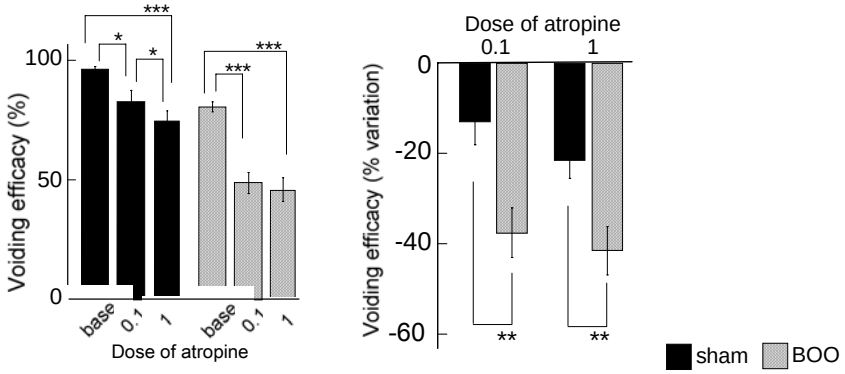


Figure 3: Voiding efficacy (%) was reduced by each dose of atropine administration in both groups. Inhibitory effect of atropine in percent variation of voiding efficacy was more pronounced in BOO.



FUNDING: NONE
DISCLOSURES: NONE
ANIMAL SUBJECTS: This study followed the guidelines for care and use of laboratory animals and was approved by Hokkaido University Institutional Animal Care and Use Committee