437

Saito M[1], Shimizu S[1], Kinoshita Y[1], Satoh I[1], Satoh K[1]
1. *Tottori University*

FUNCTIONAL AND HISTOLOGICAL CHANGES AFTER ACUTE URINARY RETENTION IN THE RAT

Hypothesis / aims of study

There are increasing evidences that benign prostatic hyperplasia (BPH) induces over active bladder (OAB) syndrome (1). However, only little information are available about bladder function after acute urinary retention (AUR). In this study, we investigated the effects of AUR on bladder function over a four-week period in a rat model.

Study design, materials and methods

All animal experiments were performed in accordance with the guidelines established by our University Committee for Animal Experimentation. Eight-week-old female Sprague Dawley rats were used in this study. AUR was induced by the clamping the rat distal urethra with a small clip, and then infusing 3 ml (0.6 ml/min) of saline with an infusion pump through transurethral catheterization (22G). The obstruction was sustained for 60 minutes and then bladder was allowed to drain with the catheter. The bladder functions were estimated by voiding behavior studies (at 3 days, 1, 2, 3 and 4 weeks), cystometric studies (under 1.0 g/kg s.c. of urethane anesthesia; saline infusion speed 12 ml/hr, at 2 and 4 weeks) and organ bath studies using KCl (100 mM) and carbachol (10^{-8}-10^{-4} M) (at 2 and 4 weeks). Furthermore, we evaluated histological changes in the rat bladder 2 and 4 weeks after the induction of AUR. The same parameters were also observed in non-AUR rats (Control group).

Results

The rat bladder weight in the AUR group at two weeks was significantly larger than that of the controls, but the rat bladder weight in the AUR group at four weeks returned to control level (Table). In the voiding behavior studies, significant increase in micturition frequency per day and decrease in single voiding volume were observed at 3 days, and this voiding behaviour was continued more than two weeks. However, no significant changes of urine output per day were observed in the experimental rats (Figure). In cystometric studies, there were no significant differences in bladder capacity, maximum detrusor pressure during voiding, single-voided volume, and residual urine volume between AUR groups and control group. In functional studies, contractions to 100 mM KCl, and E_{max} and EC_{50} values to carbachol were no significantly different among control, 2 weeks and 4 weeks rat bladder smooth muscles (Table).

Table. Bladder weight and E_{max} and EC_{50} values.

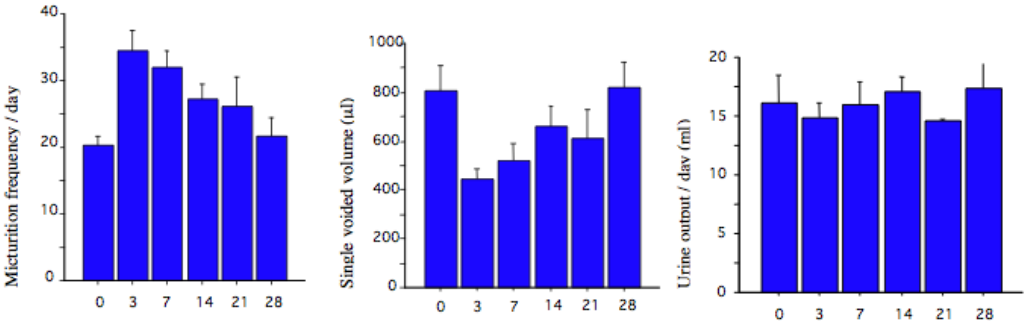
	Bladder Weight (mg)	E_{max} (g/mm2)	EC_{50} (X10-6 M)
Cont	92 ± 7	2.53 ± 0.38	1.5 ± 0.4
AUR 2 weeks	153 ± 22*	2.33 ± 0.32	2.0 ± 0.4
AUR 4 weeks	105 ± 2	2.53 ± 0.36	1.4 ± 0.1

E_{max} and EC_{50} values were for carbachol. *) significantly different from the other groups.

In histological studies, significant infiltrations of neutrophiles and lymphocytes, and increase in turnover of epithelium were observed AUR rats at 2 weeks, while significant increases in fibrosis in submucosal layer were observed AUR rats at 4 weeks.

Interpretation of results

We have reported that AUR and subsequent catheterization of the bladder caused bladder dysfunction as a result of lipid peroxidation and oxidative DNA damage of the bladder tissue (2). In the previous reports, AUR and subsequent catheterization of the bladder significantly decreased contractile response to KCl and carbachol, but there were no available information in regard to the bladder function recovery and the histological alterations of the bladder after AUR. Tammela and coworkers reported that overdistension causes a proliferative reaction within the bladder wall (3). In their reports, the initial effects of overdistention of the bladder occured within the urothelium, and the later involvement of the subendothelial smooth muscle and connective tissue were directly proportional to the degree of bladder distension three weeks following overdistension. Morover, the bladder's functional state was not completely recovered, although the urinary bladder was found to have a good capacity to adapt and compensate for the stress-induced changes caused by overdistension.



The above mentioned results are in agreement with our data. Interestingly, although bladder function was recovered within 2 weeks as estimated by organ bath studies, a significant increase in micturition frequency per day was observed by voiding behavior studies for more than 2 weeks. These findings may give a clue to understand AUR- and BPH accociated over active bladder (OAB) syndrome.

Concluding message

We demonstrated that bladder dysfunction in a rat model caused by AUR needs more than two weeks of recovery period. The AUR-associated alterations in the bladder may represent a key clue to understand OAB syndrome. The rat model may represent an adequate model for the pharmaceutical management of OAB syndrome.

References

1. J Urol. 148: 1957-61, 1992
2. J Urol. 165: 1745-47, 2001
3. J Urol. 150: 1533-9, 1993

Specify source of funding or grant	**Non**
Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**Tottori University Committee for Animal Experimentation**