

128

Authors: Hiroshi Tanaka, Hidehiro Kakizaki, Shinobu Matsuura, Takahiko Mitsui, Kaname Ameda and Tomohiko Koyanagi

Institution: Dept. of Urology, Hokkaido Univ. School of Medicine

Title: PREEMPTIVE TREATMENT OF CAPSAICIN DOES NOT PREVENT THE DEVELOPMENT OF DETRUSOR INSTABILITY FOLLOWING PARTIAL URETHRAL OBSTRUCTION IN RATS.

Aims of Study:

Partial urethral obstruction in rats produces bladder instability and hyperactive voiding. Neuroplasticity in afferent pathways including c-fiber bladder afferents is believed to be one of the major causes of such functional changes of the bladder following partial urethral obstruction [1,2]. This study was performed to determine whether capsaicin sensitive c-fiber bladder afferents are involved in the development of bladder instability following partial urethral obstruction.

Methods:

Female Wistar rats were pretreated by capsaicin (100mg/kg s.c) prior to the creation of urethral obstruction. Partial urethral obstruction was induced by placing a polyethylene catheter (PE200) around the proximal urethra. Six weeks after obstruction, micturition patterns were measured during the dark and light cycles (for 6 hours each) and parameters were compared between obstructed rats with (BO/caps, n=7) or without (BO/-, n=10) capsaicin pretreatment and age-matched sham-operated control rats (n=10). In addition, conscious filling cystometry (0.2 ml/min of saline) was performed at 6 weeks after obstruction. To evaluate the effectiveness of capsaicin pretreatment, an eye wipe test and the response to intravesical infusion of capsaicin solution (100 μ M) were also investigated.

Results:

Preliminary investigation revealed that implantation of PE200 around the proximal urethra led to a significant increase in bladder weight ($p < 0.01$). The mean bladder weight was 227.6 ± 17.9 mg in obstructed rats and 51.8 ± 3.3 mg in control rats ($n = 5$ in each group). The mean number of defensive wiping movements for 2 min in eye wipe tests was significantly different between rats with or without capsaicin pretreatment (17 in BO/- vs 3 in BO/caps, $p < 0.01$). Compared with saline infusion, intravesical infusion of capsaicin solution markedly reduced bladder capacity in BO/-, but not in BO/caps ($44.6 \pm 9.5\%$ in BO/- vs $92.0 \pm 6.8\%$ in BO/caps, $p < 0.01$). Thus, long-lasting effect of capsaicin pretreatment was confirmed. The micturition profiles showed that the average voided volume per micturition during the dark and light cycles decreased in both BO/- and BO/caps compared to control. However, these differences were not statistically significant. Compared to control, BO/caps had a significantly increased number of micturitions during the dark cycle (16.6 ± 3.0 in BO/caps vs 8.8 ± 1.5 in control, $p = 0.0306$), but not during the light cycle. The number of micturitions in BO/- was not significantly different from control. Conscious cystometry revealed that capsaicin pretreatment significantly increased bladder capacity (2.16 ± 0.23 ml in BO/caps vs 1.18 ± 0.07 ml in BO/-, $p < 0.01$) and voided volume (1.89 ± 0.22 ml vs

1.03±0.08ml, p<0.01), without changes in residual volume (0.26±0.06ml vs 0.12±0.04ml), voiding efficiency (87.8±2.3% vs 89.4±3.1%) or micturition pressure (45.0±4.9cmH₂O vs 39.4±3.2 cmH₂O). The prevalence of bladder instability was 100% in BO/caps and 83% in BO/-, and neither frequency nor amplitude of pre-micturition bladder contractions was different in both groups.

Conclusions:

Development of bladder instability and hyperactive voiding following partial urethral obstruction cannot be prevented by capsaicin pretreatment despite persistent desensitization of c-fiber afferents. These data suggest that capsaicin sensitive bladder afferents are not essential to induce bladder instability following bladder outlet obstruction in rats.

References:

1. J. Comp. Neurol. (1991) 310:401-410.
2. J. Urol. (1998) 160:34-38.