

POST-TRAUMA BLADDER MANAGEMENT STRATEGY INFLUENCES LOWER URINARY TRACT DYSFUNCTION AFTER SPINAL CORD INJURY IN THE MOUSE MODEL

Hypothesis / aims of study

Spinal cord injury (SCI) rostral to the lumbosacral level eliminates voluntary and supraspinal control of voiding, leading initially to areflexic bladder and urinary retention, and then to a development of neurogenic lower urinary tract dysfunction (LUTD) such as detrusor overactivity (DO) and inefficient voiding due to detrusor sphincter dyssynergia (DSD). Although many factors contribute to the emergence of LUTD after SCI, bladder overdistention and high storage pressure due to DSD are considered to be involved in the progress of LUTD after SCI [1]. Thus, we hypothesized that the post-trauma bladder management that reduces bladder overdistention and high pressure storage after SCI could alter the severity of SCI-associated LUTD in the later phase. In this study, we therefore examined the effects of different frequency of daily bladder squeezes (once to three times) on storage and voiding function parameters during awake cystometry in a mouse model of SCI.

Study design, materials and methods

SCI was produced by complete transection of the Th8/9 spinal cord in adult female C57BL/6N mice. After spinal transection, their bladders were manually squeezed to eliminate the urine inside every day for 4 weeks until cystometric evaluation. The mice were divided into 3 groups (n=10 in each) depending on the frequency of the bladder squeezes; A: once daily (only early morning), B: twice daily (early morning and late evening), C: three times daily (early morning, afternoon and late evening). Animals were housed in standard cages with wood-chip bedding and had free access to food and water. A 12-h light-dark cycle (lights on at 07:00 am) was used throughout. Four weeks after transection, continuous and single-filling cystometry were performed under an awake condition. We also evaluated the mRNA expression of ATP receptors (P2X2, P2X3), TRPA1 and TRPV1 of L6/S1 dorsal root ganglia (DRG) that contain bladder afferent neurons.

Results

In continuous cystometry (Figure 1), the number of non-voiding contractions (NVCs) per voiding cycle was significantly decreased as the frequency of daily bladder squeezes was increased. Postvoid residual urine (PVR) and bladder capacity were significantly less in group C (3 times squeezes) compared to group A (1 time squeeze), resulting in better voiding efficiency in group C with a significant difference ($p<0.05$) compared to group A. Also, in single cystometry, the number of NVCs per voiding cycle was significantly ($p<0.05$) decreased as the frequency of daily bladder squeezes was increased. PVR and bladder capacity were significantly less ($p<0.05$) in group C than in group A. Voiding efficiency was better when the frequency of daily bladder squeezes was increase; but there were no statistical significances.

The expression of mRNA (Figure 2) of P2X2, P2X3, TRPA1, and TRPV1 was increased ($p<0.05$) in SCI mice compared to spinal intact mice (n=7). The expression of P2X3 and TRPA1 in groups B and C were decreased ($p<0.05$) compared to group A. The expression of P2X2 was also decreased in groups B ($p<0.05$) compared to group A. TRPV1 was decreased in group B and C; but there were no statistical significances.

Interpretation of results

The frequency of daily bladder squeezes after spinal cord injury greatly affect storage and voiding dysfunction and the expressions of P2X receptors or TRP channels of DRG after SCI. In SCI mice receiving three times squeezes daily, the emergence of NVCs was less compared to SCI mice with once or twice daily of squeezes. Similarly, PVR was less and the voiding efficiency was better in three times squeezed SCI mice. These results are consistent with the clinical findings that bladder deterioration is better controlled in patients with neurogenic bladder who are performing intermittent catheterization more frequently [1]. The expression of P2X2, P2X3, TRPA1 and TRPV1, which are predominantly expressed in C-fiber afferent pathways, was higher in L6/S1 DRG of SCI mice compared to spinal intact mice. In SCI mice receiving twice or three times squeezes daily, these increased expressions were reduced with the significant differences of P2X3 and TRPA1 in group B and C, and of P2X2 in group B compared to group A, suggesting that more frequent bladder emptying after SCI could reduce the C-fiber afferent hyperexcitability underlying LUTD after SCI.

Concluding message

These results indicate that the post-trauma bladder management with increased frequency of daily bladder emptying improves the storage and voiding LUTD after SCI, as evidenced by the reduction in NVCs and PVR, respectively, in the three-times bladder squeezed group, and that the improvement of SCI-induced LUTD is associated with the reduction of C-fiber afferent marker receptors in bladder afferent pathways. Thus, it is assumed that the well-planned initial management strategy would be important for the control of LUTD that develops after the initial areflexic phase of SCI. Also, in the basic LUTD research, researchers should consider the tailored plan of animal care of chronic disease models after surgical manipulation depending on their intended purposes.

Figure 1: Parameters in continuous cystometry

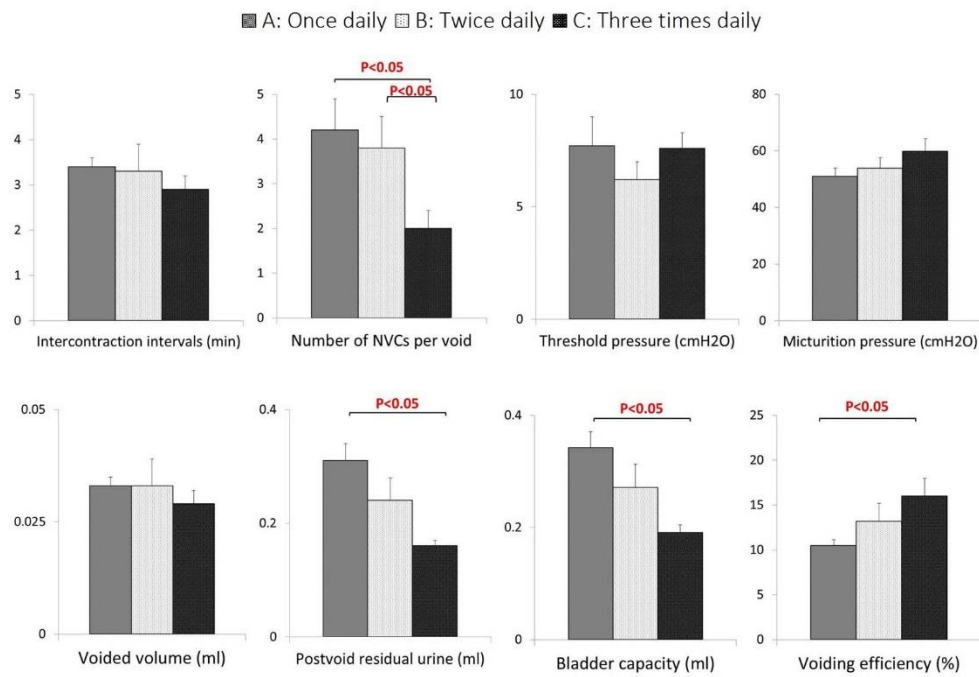
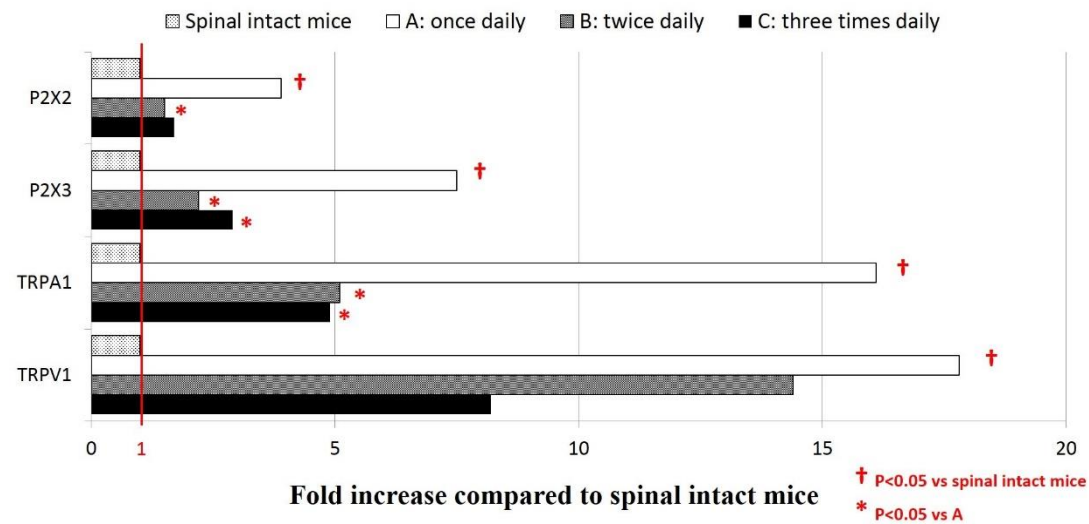


Figure 2: mRNA expressions in DRGs (L6/S1)



References

1. Yokoyama O et al. J Urol 1996; 155: 271-274.

Disclosures

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