

## THE ANTAGONIST OF TRANSIENT RECEPTOR POTENTIAL CHANNEL A1-HC030031 INHIBITS THE HYPER-REFLEXIC MICTURITION OF CYCLOPHOSPHAMIDE-INDUCED CYSTITIS MODEL OF RATS.

### Hypothesis / aims of study

Transient receptor potential channel (TRP) A1 is expressed in the afferent pathway of urinary bladder (1). It is involved in the mechanic transduction, nociception and cold sensation. We investigated its expression in the cyclophosphamide-induced cystitis in rats and its role in the hyper-reflexic micturition of cystitis model.

### Study design, materials and methods

The cystitis was induced by intraperitoneal injection of cyclophosphamide (350 mg/kg) in rats. The urinary bladder and dorsal root ganglia (DRG) innervating the bladder were harvested 3 days later. The expression of TRPA1 was analyzed by quantitative real-time RT-PCR. The cystometry was performed in urethane anesthetized rats. The role of TRPA1 was investigated by intrathecal injection of its antagonist HC-030031. The data was analyzed by paired t-test and t-test.

### Results

The intraperitoneal injection of cyclophosphamide induced cystitis 3 days after injection. The expression level of TRPA1 was not obviously changed in either urinary bladder or DRG. For the cystometry using cystitis model, the inter-contraction interval was  $2.38 \pm 0.52$  and  $4.63 \pm 1.76$  minutes, respectively ( $p < 0.05$ ,  $n=4$ ), before and after the intrathecal injection of  $50 \mu\text{g}$  HC-030031. The number of non-voiding contraction was  $3.75 \pm 1.71$  and  $2 \pm 1.41$  times, respectively ( $p < 0.05$ ). The compliance was  $7.37 \pm 3.46$  and  $14.75 \pm 5.95 \mu\text{L/mmHg}$ , respectively ( $p < 0.05$ ). It usually took 30 minutes for HC-030031 to show effects. These effects became weak 2 hours later. The micturition pressure, baseline pressure and pressure threshold were not changed significantly. The intrathecal injection of HC-030031 did not show obvious effect on the cystometry parameters in normal rats.

### Interpretation of results

The expression of TRPA1 mRNA is not changed in the acute cystitis model of rats. The intrathecal injection of HC-030031 did not affect the contractile ability of rat urinary bladder. Even though there was no change in the expression level of TRPA1 in DRG, the intrathecal injection of HC-030031 did inhibit the hyper-reflexic micturition of cystitis model by increasing the inter-contraction interval and inhibiting the non-voiding contraction.

### Concluding message

As a nociceptor, TRPA1 might be involved in the increased activity of afferent pathway in pathologic condition such as inflammation. TRPA1 is a possible target for the treatment of overactive bladder, especially those related with inflammation or bladder pain.

### References

1. Du S, Araki I, Yoshiyama M, Nomura T, Takeda M. Transient receptor potential channel A1 involved in sensory transduction of rat urinary bladder through C-fiber pathway. *Urology*, 2007 Oct; 70(4):826-31.

### Disclosures

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