480

Ishiura Y. [1], Yoshiyama M. [2], Yokoyama O. [3], Namiki M. [1], de Groat W. [2]
1. Kanazawa University, 2. Pittsburgh University, 3. Fukui Medical University

INFLUENCE OF THE SPINAL MUSCARINIC SYSTEM VIA C-FIBER AFFERENT ON BLADDER OVERACTIVITY IN PATHOLOGICAL BRAIN MODELS

Aims of Study

Pathological brain models such as cerebral infarcted rats and decerebrated rats reveal decrease in bladder capacity, indicating bladder overactivity (1), (2). This overactivity has been attributed to the interruption of inhibitory pathways from the forebrain to the pontine micturition center. We previously reported that oxotremorine-M (OXO-M), a nonselective muscarinic receptor agonist, influence the spinal processing of C-fiber input from the bladder afferent (3), (4). The present study was undertaken to examine whether bladder overactivity caused by pathological brain could be suppressed by activation of the spinal muscarinic systems.

Methods

Under halothane anesthesia, cystometry catheter and intrathecal (it) cannula were inserted into the bladder and spine in female SD rats (250 - 300g), respectively. Cerebral infarction was induced by left middle cerebral artery occlusion (5). A precollicular decerebration was performed according to published methods (6). The brain rostral to the superior colliculus was removed with a blunt spatula. Bladder activity was monitored with continuous infusion cystometrography without anesthesia. Saline was infused into the bladder at a constant rate (0.1 ml / min). Increasing doses of OXO-M (0.001 – 1 μg / rat, it) were injected in three groups; normal rats, cerebral infarcted rats, decerbrated rats.

Results

Bladder capacity after cerebral infarction and decerebration significantly decreased when compared to bladder capacity before these procedures. Bladder capacity before intrathecal OXO-M injection, which was regarded as control in normal rats, cerebral infarcted rats and decerebrated rats, were 0.35 0.03 ml, 0.22 0.02 ml and 0.33 0.03 ml respectively. Increasing doses of intrathecal OXO-M increased bladder capacity dose dependently in each group. Bladder capacity after 0.1 μg of OXO-M injection in normal rats, cerebral infarcted rats and decerebrated rats were 0.64 0.10 ml, 0.32 0.04 ml and 0.52 0.05 ml respectively. Percentage changes in bladder capacity after 0.1 μg of OXO-M injection in normal rats, cerebral infarcted rats and decerebrated rats were 84.6 17.1 %, 51.1 20.5 % and 65.9 20.4 % when compared to pre-injection capacity. Furthermore, changes in bladder capacity after 1 μg of OXO-M injection in normal rats, cerebral infarcted rats and decerebrated rats were 179.0 ± 20.5 %, 98.0 19.5 % and 97.0 22.3 %. Percentage increases in bladder capacity of normal rats were significantly higher than those of cerebral infarcted rats or decerebrated rats.

Conclusions

The present study revealed that intrathecal OXO-M caused an increase in bladder capacity in normal and pathological brain rats. However, degree of increase in bladder capacity of pathological brain models is smaller than that of normal rats. These results indicate that the spinal muscarinic inhibitory system via C-fiber input from the bladder afferent might be downregulated in bladder overactivity caused by the pathological brain.

References

1. Yokoyama O, Komatsu K, Ishiura Y, Nakamura Y, Morikawa K and Namiki M: Change in bladder contractility associated with bladder overactivity in rats with cerebral infarction. J Urol 159: 577-580, 1998.
2. Yokoyama O, Yoshiyama M, Namiki M and de Groat WC: Role of the forebrain in bladder overactivity following cerebral infarction in the rat. Experimental Neurology 163: 469-476, 2000.
3. Ishiura Y, Yoshiyama M, Yokoyama O, Namiki M and de Groat WC: Central muscarinic mechanisms regulating voiding in rats. J Pharmacol Exp Therapeu 297: 933-939, 2001.
4. Ishiura Y, Yoshiyama M, Yoshimura N, Yokoyama O, Namiki M and de Groat WC: Effects of intrathecal oxotremsorine-M on bladder hyperactivity induced by acetic acid irritation in awake rats. Neurourol and Urodynam 20: 374-375, 2001.
5. Longa EZ, Weinstein PR, Carlson S and Cummins R: Reversible middle cerebral artery occlusion without craniectomy in rats. Stroke 20: 84-91, 1989
6. Sapru HN and Krieger AJ: Procedure for the decerebration of the rat. Brain Res. Bull. 3: 675-679, 1978.