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EFFECTS OF SOLIFENACIN SUCCINATE ON DETRUSOR OVERACTIVITY IN CONSCIOUS CEREBRAL INFARCTED RATS

Hypothesis / aims of study

Solifenacin succinate is a newly synthesized muscarinic receptor antagonist, and widely used for the treatment of overactive bladder syndrome. Pharmacological studies have demonstrated that solifenacin has muscarinic inhibitory effects on bladder smooth muscle in vitro and vivo animal experiments (1,2). However, there are few reports about the effects of solifenacin on detrusor overactivity in animal model. A rat model of detrusor overactivity associated with cerebral infarction and characterized by decreased bladder capacity has been developed (3). In the present study, we evaluated the effects of solifenacin on detrusor overactivity in the cerebral infarcted rat model.

Study design, materials and methods

Male Sprague-Dawley rats (270-320 g) were used. A polyethylene catheter for cystometry was inserted through superior aspect of the bladder and fixed in place. Cerebral infarction was induced according to the intraluminal suture occlusion method. Briefly, a 3-0 nylon monofilament suture was introduced through the external carotid artery into the internal carotid artery. The suture was advanced approximately 17 mm intracranially from the common carotid artery bifurcation to block the origin of the middle cerebral artery. One day after middle cerebral artery occlusion, cystometry was performed. Intravesical pressure was recorded by infusing saline into the bladder, and the volume of urine voided from the urethral meatus was measured to determine the voided volume. After stable voiding cycles were established, each rat received a single intravenous administration of test drugs (solifenacin succinate, tolterodine tartrate and propiverine hydrochloride). Rats were randomly assigned to one of each treatment groups (n=8) Data were expressed as the mean ± S.E.M.

Results

The cerebral infarcted rats showed a significant decrease in bladder capacity and voided volume (0.83 ± 0.03 mL and 0.54 ± 0.03 mL, respectively) compared to the sham-operated rats (1.32 ± 0.08 mL and 1.20 ± 0.09 mL, respectively). Solifenacin (0.01-0.3 mg/kg) dose-dependently increased bladder capacity and voided volume at doses of 0.03 mg/kg i.v. or more, but did not affect residual volume or micturition pressure at any dose tested. Tolterodine (0.01-0.1 mg/kg) also dose-dependently increased bladder capacity and voided volume at 0.03 and 0.1 mg/kg i.v., but did not affect residual volume or micturition pressure at any dose tested. Further, propiverine (0.03-1 mg/kg) tended to increase bladder capacity at 0.3 mg/kg i.v. (p=0.09) and significantly increased it at 1 mg/kg i.v., and dose-dependently increased voided volume at 0.3 and 1 mg/kg i.v., but did not affect residual volume or micturition pressure at any dose tested.

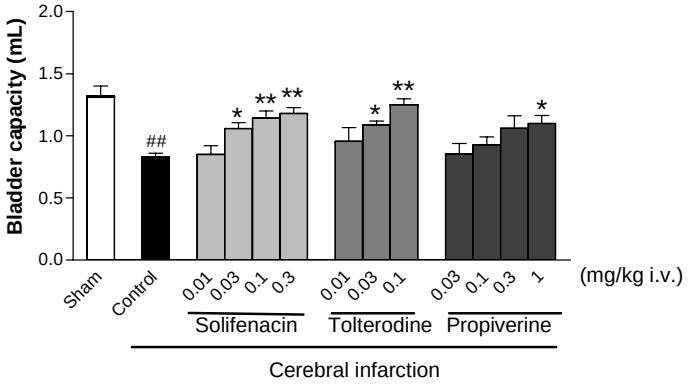

Fig. 1 Effects of solifenacin, tolterodine and propiverine on bladder capacity in cerebral infarcted rats. Each column represents the mean ± S.E.M. of 8 rats. ## p<0.01: significant

difference to the sham-operated group (Student's t test). * $p<0.05$, **$p<0.01$: significant difference to the control group (Dunnett's multiple comparison test).

Interpretation of results

In a rat model of cerebral infarction induced by middle cerebral artery occlusion, detrusor overactivity was observed, which illustrated by significant decrease in bladder capacity. In the cerebral infarcted rat, solifenacin improved detrusor overactivity without causing urinary retention as well as tolterodine and propiverine. Solifenacin and tolterodine showed the improving effects on detrusor overactivity at lower doses than propiverine.

Concluding message

Solifenacin ameliorated the detrusor overactivity induced by cerebral infarction without causing urinary retention in a rat model. These findings suggest that solifenacin may be a promising drug in patients with overactive bladder syndrome including urgency frequency, and incontinence.

References

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