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EFFECT OF GENETICIN ON THE BLADDER DYSFUNCTION AND CEREBRAL INFARCTION AFTER THE EXPERIMENTAL STROKE

Aims of Study

After cerebral ischemia serious neurological deficits in motor function, speech, vision, memory and voiding control are common. Specifically damage to the neural circuitry in the forebrain may produce bladder dysfunction and urinary incontinence. According to previous reports cerebrovascular disease causes urinary dysfunction in about 20% to 50% of all patients. Thus, urinary incontinence is a serious problem in cerebrovascular disease survivors. The control of micturition by the brain is imperfectly understood. As previously described, the frontal lobe is largely responsible for urinary tract function. An experimental model of the influence of forebrain lesions on voiding function has recently been developed by occluding the middle cerebral artery (MCAO) in rats.

In a myocardial infarction model using rats, antibiotic geneticin reduced infarct volume under both ischemia only and ischemia followed by reperfusion (ischemia-reperfusion) conditions when administered before ischemic onset.

In this study, we evaluated the effect of the geneticin on the bladder dysfunction and cerebral infarction using experimental model of stroke.

Methods

We implanted bladder catheter to the male Sprague-Dawley rats. Cystometrogram was obtained 7 days after implantation as control. Normal saline was infused into the bladder at a constant rate (200 microl. per minute) and a cystometrogram was obtained while the rats are in the conscious state.

Cerebral infarction was made by occluding left middle cerebral artery with 3-0 monofilament nylon thread for 90 minutes. 1 and 3 days after the induction of cerebral ischemia, cystometrogram was repeated and rats were sacrificed immediately after the final cystometrogram.

Geneticin (50 mg/kg) was injected intraperitoneally 1 hour before, 1 and 3 hours after ischemic onset.

To estimate the degree of infarction, we performed triphenyl tetrazolium chloride (TTC) staining of the brains and measured the area of damage using image analysis system.

Results

After middle cerebral artery occlusion, bladder capacity in conscious rats was reduced (sham [n=6]: 138.5% of control, MCAO [n=8]: 110.1% of control) and bladder contractility was increased (sham [n=6]: 95.4% of control, MCAO [n=8]: 151.7% of control) compared to the sham operated rats. Geneticin treatment significantly attenuated the enhanced contractility after ischemia (MCAO [n=8]: 151.7% of control, geneticin [n=5]: 89.3% of control) but did not affect the bladder capacity after ischemia. Geneticin itself decreased bladder capacity up-to 3 days after treatment in sham-operated animals (73.5% of control, n=5). Geneticin treatment also inhibited the neuronal damage caused by middle cerebral artery occlusion (geneticin [n=5]: 30.4% of ipsilateral hemisphere, vehicle [n=8]: 70.8% of ipsilateral hemisphere).

Conclusions

Transient occlusion of middle cerebral artery induced focal ischemic damage of the brain and bladder dysfunction in rats. Geneticin treatment reduced infarct size and attenuated urinary dysfunction when treated immediately before and after ischemic onset. Our results suggest that under ischemic conditions, geneticin function as a neuroprotective agent and thus can be used as a therapeutic agent to treat ischemic disease and bladder dysfunction.