

INFLUENCE OF PROPIVERINE, AN ANTICHOLINERGIC AGENT, ON MICTURITION REFLEX, BLOOD PRESSURE, AND PLASMA CATECHOLAMINE LEVEL IN YOUNG AND ELDERLY RATS

Hypothesis / aims of study

Anticholinergic agents inhibit the parasympathetic nerve activity by inhibit to the interaction of acetylcholine and acetylcholine receptor. Therefore, they can be called parasympathetic blocker, and have a possibility to relatively stimulate the sympathetic nerve activity. Generally, it has been reported that plasma catecholamine level increases with age. Catecholamine level is related to the bladder activity via effect to the spinal cord and blood pressure, etc. Therefore, we examined the influence of propiverine hydrochloride, an anticholinergic agent, on micturition reflex, blood pressure, and plasma catecholamine level in young rats and elderly rats.

Materials and methods

Forty male F344/DuCrj Fischer rats (young rat: 2 month old. elderly rat: 26 month old) were used in this study. Rats were divided into 4 groups; a young sham group (n=10), an elderly sham group (n=10), a young propiverine group (n=10), and an elderly propiverine group (n=10). Rats from the young propiverine group and the elderly propiverine group were administered 5 mg of propiverine hydrochloride dissolved in distilled water (0.5 mL) in the morning using a fine catheter without anaesthesia. These doses correspond to about 20 times the human dosage. Rats from the young sham group and the elderly sham group were administered the same volume of distilled water once a day. After 2 weeks of treatment, we performed 2 examinations as following; Study 1: Twenty rats (5 from each group) were anesthetized with urethane and were placed in a supine position. Then a polyethylene catheter was inserted into the bladder dome to perform continuous cystometry. Physiological saline was infused into the bladder (0.05 ml/min) via the catheter and bladder activity was monitored. After cystometry was done with physiological saline, rats also underwent continuous cystometry with a 0.1% acetic acid solution. Cystometry was performed for at least 60 min with each solution, and the changes of bladder activity were recorded. Study 2: Other 20 rats (5 from each group) were determined the blood pressure by the tail-cuff method using a programmed sphygmomanometer. After blood pressure measurement (2 days later), same rats were anesthetized with urethane, and blood was withdrawn from vena cava to measure the plasma catecholamine (adrenaline, noradrenaline, and dopamine) levels. Results are reported as the mean \pm standard deviation (SD). Student's unpaired t-test was used for statistical analysis, and $p < 0.05$ was considered to indicate statistical significance

Results

Study 1: Comparison of the young sham group and the elderly sham group. During continuous cystometry with physiological saline, the interval of bladder contractions was significantly ($p < 0.001$) longer in the elderly sham group than that in the young sham group. When continuous cystometry was done with acetic acid, the interval of bladder contractions was significantly shorter than those obtained with physiological saline in both the young sham group ($p = 0.012$) and the elderly sham group ($p < 0.001$). There were no significant differences in the maximum bladder contractions pressure and intravesical baseline pressure between the young sham group and the elderly sham group. On the plasma catecholamine level, noradrenaline and dopamine were significantly ($p = 0.002$ and $p = 0.033$) higher in the elderly sham group than those in the young sham group. However, significant difference of blood pressure was not observed between these sham groups.

Study 2: Comparison of the young propiverine group and the elderly propiverine group. During continuous cystometry with physiological saline, the interval of bladder contractions was significantly ($p = 0.020$) longer in the elderly propiverine group than that in the young propiverine group. When continuous cystometry was done with acetic acid, the interval of bladder contractions was significantly ($p = 0.031$) shorter than that obtained with physiological saline in the young propiverine group, but not in the elderly propiverine group. Compared with interval of bladder contractions between the young propiverine group and the elderly propiverine group in cystometry with acetic acid, it was significantly ($p = 0.010$) longer in the elderly propiverine group than that in the young propiverine group. Between the young sham group and the young propiverine group, significant differences in cystometric parameter were not observed. However, the interval of bladder contractions in cystometry with acetic solution in the elderly propiverine group was significantly ($p = 0.026$) longer than that in the elderly sham group. On the plasma catecholamine level, noradrenaline and dopamine were significantly ($p < 0.001$ and $p = 0.003$) higher in the young propiverine group than those in the young sham group. However, plasma catecholamine levels did not change between the elderly sham group and the elderly propiverine group. Significant difference of blood pressure was also not observed between these propiverine groups.

Interpretation of results

Elderly rats have the long interval of bladder contractions and the high plasma catecholamine levels compared with the young rats. Bladder stimulation by 0.1% acetic acid induced urinary frequency in both young and elderly rats. However, administration of propiverine inhibited the urinary frequency induced by bladder stimulation in the elderly rats. In the young rats, propiverine increased the plasma catecholamine levels. Catecholamine levels may not be increased by administration of propiverine in the elderly rats probably because the catecholamine levels were already high at the elderly rats.

Concluding message

Propiverine inhibited the urinary frequency. In the young rats, propiverine increases the plasma catecholamine level without increase of blood pressure in the young rats. In the elderly rats, propiverine does not increase the plasma catecholamine level and blood pressure.

Specify source of funding or grant

none

Is this a clinical trial?

No

What were the subjects in the study?

ANIMAL

*Were guidelines for care and use of laboratory animals followed
or ethical committee approval obtained?* Yes

Name of ethics committee

Institutional animal care and use committee of the University of
the Ryukyus
