

THE SHORT- AND LONG TERM EFFECTS OF A SINGLE DOSE OF APOMORPHINE ON MICTURITION FUNCTION IN UNI- AND BI-LATERAL 6-HYDROXYDOPAMINE TREATED PARKINSON'S DISEASE MODEL RATS

Hypothesis / aims of study

The effect of anti-parkinsonian drugs (levodopa and dopamine agonist) on micturition has been controversial, because previous reports showed that anti-parkinsonian drugs aggravated and alleviated micturition disturbance in patients with Parkinson disease (PD), and accelerated and inhibited micturition reflex in experimental models. These studies did not, however, consider the time course effect of a single dose, and this may account for the conflicting findings. We, therefore, investigate the short- and long-term effects of a single dose of apomorphine, which is one of anti-parkinsonian drugs (dopamine agonist), on micturition function in uni- and bi-lateral 6-hydroxydopamine treated PD model rats.

Study design, materials and methods

Experiments were performed on adult male Sprague-Dawley rats (8 weeks) in standardized environmental conditions. 4 weeks before studies, uni- and bi-lateral injections of 6-hydroxydopamine (6OHDA) (PD model) or saline (Sham model) were performed in substantia nigra stereotaxically. 7 days before studies, a polyethylene tube (PE-50) was inserted into the bladder from the bladder dome with midline abdominal incision. 3 days before studies, animals were attached on harness with external tube, and kept in metabolic cages in order to settle in to study's condition. Studies were performed in the evening. Number of micturition per 15 minutes, urine volume per void, and cystometrograms were measured continuously in awake and free moving rats. After achievement of equilibration and 30-60 minutes' baseline recording, a single dose of apomorphine (low dose: 0.01, middle dose: 0.05, high dose: 0.5 mg/kg) or a same volume of saline was given subcutaneously, and recording was continued for over 4 hours after drug administration. The data obtained in each condition were compared with each other.

Results

In baseline recordings, number of micturition per 15 minutes and urine volume per void were severer with the increase in the number of 6OHDA treated lesion (bilateral PD > unilateral PD > sham models). In saline-administrated uni-/bi-lateral PD and sham model rats, number of micturition per 15 minutes, urine volume per void, and cystometrograms almost unchanged from the base line. In apomorphine-administrated rats, a low dose (0.01 mg/kg) induced a decrease in the number of micturition per 15 minutes and an increase in urine volume per void throughout over 240 minute's period (bilateral PD > unilateral PD > sham models). A middle (0.05 mg/kg) and high (0.5 mg/kg) dose induced an increase in the number of micturition per 15 minutes and a decrease in urine volume per void for in the first several minutes, together with increase in detrusor instability, spontaneous detrusor pressure and pre-micturition detrusor pressure (a short-term effect) (bilateral PD unilateral PD sham models), and it induced a decrease in the number of micturition per 15 minutes and an increase in urine volume per void for in the following several minutes (over 200 minutes) (a long-term effect) (sham unilateral PD or bilateral PD models). High dose administration caused more significant change.

Interpretation of results

In both PD and sham model rats, comparing apomorphine-administrated rats to saline-administrated rats, time-course dependent biphasic changes were observed. These changes slightly depended on the number of 6OHDA treated lesion.

Concluding message

Apomorphine, which is one of anti-parkinsonian drugs (dopamine agonist), has biphasic effects on micturition reflex of PD model rats depending on the time-course of a single dose, and these changes were slightly different in accordance with the severity of the brain lesion. This may account for the previously conflicting reports on the effects of anti-parkinsonian drugs on micturition disturbance in patients with PD.

DISCLOSURES: NONE

ANIMAL SUBJECTS: This study followed the guidelines for care and use of laboratory animals and was approved by Chiba university