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Uchiyama T[1], Sakakibara R[1], Yoshiyama M[2], Liu Z[1], Yamanishi T[3], Hattori T[1]
1. Department of Neurology, Chiba University Graduate School of Medicine, 2. Department of Urology, Yamanashi University Graduate School of Medicine & Engineering, 3. Department of Urology, Dokkyo Medical College

THE SHORT- AND LONG-TERM EFFECTS OF A SINGLE DOSE OF APOMORPHINE ON MICTURITION FUNCTION IN CONSCIOUS AND FREE MOVING 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 or alleviated micturition disturbance in patients with Parkinson disease, and accelerated or inhibited micturition reflex in experimental models. These studies did not, however, consider the effects of time course 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 awake and free moving rats.

Study design, materials and methods

Experiments were performed on adult male Sprague-Dawley rats (250-300g) in standardized environmental conditions. At 7 days before studies, a polyethylene tube (PE-50) was inserted into the bladder from the bladder dome with midline abdominal incision under nembutal anesthesia. At 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 recorded 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 each other.

Results

In saline-administrated rats, number of micturition per 15 minutes, urine volume per void, and cystometrograms almost unchanged. 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. 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 up to 80 minuets after drug administration (a short-term effect), and it induced a decrease in the number of micturition per 15 minutes and an increase in urine volume per void for up to 230 minutes from 80 minutes after drug administration (a long-term effect). High dose administration caused more significant change than middle dose administration. Middle and high dose administration also showed significant changes in detrusor overactivity, maximum detrusor pressure and premicturition detrusor pressure for up to 80 minutes after drug administration (a short-term effect).

Interpretation of results

Comparing apomorphine-administrated rats to saline-administrated rats, time-course dependent biphasic changes were observed. These changes depended on the administration dose.

Concluding message

Apomorphine, which is one of anti-parkinsonian drugs (dopamine agonist), has biphasic effects on normal micturition reflex depending on the time-course of a single dose. This may account for the previously conflicting reports on the effects of anti-parkinsonian drugs on micturition.