Pharmacological mechanisms of ameliorating effects of cloperastine on urinary disturbance caused by cerebral infarction

○Gen Yamamoto, Fumio Soeda, Tetsuya Shirasaki and Kazuo Takahama
(Dept. Environ. & Molec. Health Sci., Grad. Sch. Pharm. Sci., Kumamoto Univ.)

Intraluminal occlusion of the middle cerebral artery, which produces overactive bladder (OAB) and dysuria, has been introduced as a useful model of stroke-induced urinary disturbances. Using this model, we have recently found that cloperastine (CP), a centrally acting antitussive, ameliorated OAB and dysuria in conscious rats after 24 h of cerebral infarction (CI). CP has a potent inhibitory effect on G-protein coupled inwardly rectifying K^+ (GIRK) channel-activated currents. It has been well known that GIRK channels are coupled with various receptors including 5-HT_{1A} receptors. There have also been some reports that 5-HT are involved in micturition reflexes. Therefore, we investigated whether serotonin and/or 5-HT_{1A} receptor involved in the effects of cloperastine on urinary disturbances after CI, using the specific serotonin depletory (PCPA), selective 5-HT_{1A} receptor agonist (8-OH-DPAT) and antagonist (WAY100635).
【Results】PCPA (200mg/kg, s.c.) inhibited the ameliorating effects of cloperastine on OAB and dysuria in conscious rats after 24 h of CI. Interestingly, 8-OH-DPAT (0.3mg/kg, i.v.) ameliorated OAB and dysuria associated with CI as well as cloperastine. The effects of 8-OH-DPAT were completely inhibited by WAY100635 (0.3mg/kg, i.v.) pretreatment. The ameliorating effect of cloperastine on OAB was inhibited by WAY100635, whereas the effect on dysuria was not inhibited. These results suggest that the ameliorating effects of cloperastine on OAB and dysuria in rats with CI may result at least partly from an increase of 5-HT release via the inhibition of GIRK channels, and further that 5-HT_{1A} receptor may be involved at least partly in production of the effects of cloperastine.