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γ-Aminobutyric acid attenuates monocrotaline-induced pulmonary hypertension by suppressing sympathetic nervous system but not cardiac ET-1 system

Rie Suzuki, Mamoru Ohkita, Yasuo Matsumura. Osaka University of Pharmaceutical Sciences, Pharmacology, 569-1094, Japan.

It has been reported that activation of the sympathetic nervous system and increase in plasma norepinephrine (NE) levels are observed in pulmonary hypertension (PH) patients. In the pilot study, we found that γ-aminobutyric acid (GABA), one of the major inhibitory neurotransmitters in the central nervous system and peripheral sympathetic neurotransmission, has preventive effect on monocrotaline (MCT)-induced PH in rats. Therefore, we investigated whether the reduction of plasma NE level is involved in the above GABA's action on MCT-induced PH. After MCT (60 mg/kg, s.c.) injection, animals showed time-dependent increases in right ventricular (RV) systolic pressure (RVSP), RV hypertrophy, pulmonary arterial medial thickening, and plasma NE level. Plasma NE levels were positively correlated with the increased RVSP. GABA treatment (500 mg/kg/day for 4 weeks, p.o.) suppressed the elevated plasma NE level and pulmonary hypertensive lesions in MCT-treated rats. RV endothelin-1 (ET-1) content was significantly increased in the MCT-treated animals, but this increment was not affected by the treatment with GABA. These results suggest that the increase in plasma NE levels plays an important role in the development of MCT-induced PH in rats and that GABA exerts a preventive effect against MCT-induced PH by suppressing sympathetic nervous system but not cardiac ET-1 system.