



Role of nitric oxide in the development of tolerance to diazepam-induced motor impairment in mice

Sylvia Talarek, Joanna Listos, Sylvia Fidecka

Department of Pharmacology and Pharmacodynamics, Medical University of Lublin, Staszica 4,
PL 20-081 Lublin, Poland

Correspondence: Sylvia Talarek, e-mail: sylvia.talarek@am.lublin.pl

Abstract:

Chronic treatment with the benzodiazepines is well known to produce tolerance, which has been extensively documented to be attributed to modifications in the γ -aminobutyric acid (GABA)ergic neurotransmission. However, literature data have also suggested the participation of different neurotransmitter systems, including glutamatergic, in benzodiazepine tolerance. The purpose of the present study was to determine the role of nitric oxide (NO) in the development of tolerance to the motor dysfunction induced by chronic administration of diazepam. The motor performance was assessed on the 1st and 10th day of experiment, using the rotarod and chimney tests in mice. Treatment of animals with both non-selective NO synthase (NOS) inhibitors: N^G-nitro-L-arginine methyl ester (L-NAME), N^G-nitro-L-arginine (L-NOARG) and selective NOS inhibitor: 7-nitroindazole was able to prevent the development of tolerance to the motor impairing effect of diazepam. Moreover, administration of L-arginine, a NO precursor, facilitated the development of diazepam-induced tolerance in rotarod test. These findings suggest that NO may be involved, at least in part, in the tolerance to the motor dysfunction, developed during the chronic administration of diazepam in mice.

Key words:

nitric oxide, diazepam, tolerance, motor impairment, mice
